

EXHIBIT D

CONFIDENTIAL

Abatement Strategies for Addressing the Opioid Crisis

Expert Witness Report of G. Caleb Alexander, MD, MS

August 22, 2022

CONFIDENTIAL

Contents

I. Background and Qualifications of Author	4
II. Data Sources, Methodology, and Opinions	7
III. Opioid Crisis Indicia and National Abatement Efforts	9
IV. Principles Governing Effective Response	11
V. Abatement Framework	12
Category 1: Prevention – Reducing Opioid Oversupply and Improving Safe Opioid Use	14
A. Health Professional Education	14
B. Patient and Public Education	20
C. Safe Storage and Drug Disposal	22
D. Harm Reduction	24
E. Prescription Drug Monitoring Programs	27
F. Community Prevention and Resiliency	28
G. Leadership, Surveillance, and Implementation	30
Category 2: Treatment – Supporting Individuals Affected by the Epidemic	33
A. Connecting Individuals to Care	33
B. Treatment for Opioid Use Disorder	37
C. Addressing Non-Medical Opioid Use	42
D. Managing Complications Attributable to the Epidemic	45
E. Workforce Expansion and Resiliency	48
F. Distributing Naloxone and Providing Training	52
Category 3: Recovery – Enhancing Public Safety and Reintegration	54
A. Public Safety	54
B. Criminal Justice System	56
C. Vocational Training	59
D. Mental Health and Grief Support	61
Category 4: Addressing Needs of Special Populations	64
A. Pregnant Women, New Mothers, and Infants	64
B. Adolescents and Young Adults	67
C. Families and Children	69
D. Older Adults	71
E. Black, Indigenous, and People of Color (BIPOC)	73
F. Individuals Experiencing Homelessness and Housing Insecurity	76
G. Individuals with Complex Pain	79
VI. Measuring the Success of Abatement Efforts	81
VII. Estimated Impact of Proposed Abatement Remedies	82
VIII. Potential Objections to Proposed Abatement Remedies	84
IX. Conclusions	87
X. References	88

CONFIDENTIAL

Appendices

Appendix A – Johns Hopkins Report: “From Evidence to Impact”

Appendix B – Curriculum Vitae

Appendix C – Expert Witness Engagements

Appendix D – Materials Relied Upon

Appendix E – Potential Indicators of High-Risk Opioid Distribution

Appendix F – Transmucosal Immediate-Release Fentanyl (TIRFs) Risk Evaluation and Mitigation Strategy (REMS) Program

Appendix G – Preserving and Providing Access to Opioid Litigation Documents for the Public Good

CONFIDENTIAL

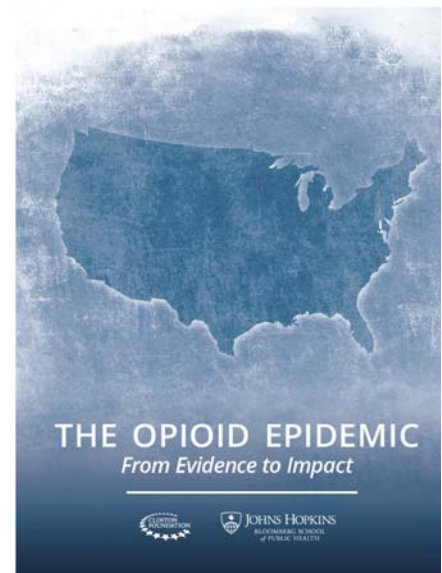
I. BACKGROUND AND QUALIFICATIONS OF AUTHOR

1. My name is G. Caleb Alexander. I am a practicing general internist and Professor of Epidemiology and Medicine at Johns Hopkins Bloomberg School of Public Health. I have been retained by Plaintiffs to provide my scientific expertise regarding how to abate or reduce the harms caused by opioid epidemic in the United States. Thus, rather than focus on one specific community, in this report I discuss the scientific foundation and rationale for programs and services as they may be applied in numerous cities, counties and states around the United States.
2. As a physician, I am responsible for the primary care of approximately 250 patients, most of whom live in and around Baltimore County. I have clinic one half-day per week and I am also responsible for patient care matters that arise at other times. The patients that I see range from young adults to nonagenarians (aged 90 – 99 years), and as a primary care physician I oversee their acute, preventive, and chronic needs, which include conditions such as asthma, diabetes, hypertension, osteoporosis, chronic pain, anxiety, and depression. While I do not specialize in the care of patients with opioid use disorder (OUD), I have patients in my practice with OUD who I co-manage with addiction specialists, and I care for patients who have lost family members to fatal opioid overdoses.
3. In contrast to my work as a physician, as a pharmacoepidemiologist, I focus on “the study of the uses and effects of drugs in well-defined populations.”¹ Pharmacoepidemiology is a bridge discipline that combines insights and tools from clinical medicine, pharmacology, and epidemiology to generate fundamental new knowledge regarding the utilization, safety, and effectiveness of prescription drugs. It also concerns itself with understanding the effects of pharmaceutical policy, such as regulatory or payment policies that influence prescription drug use. As a pharmacoepidemiologist, much of my work has focused on the nature, quality, and determinants of prescription drug utilization in the United States, although I have also conducted or participated in many investigations examining the safety of specific products. I have used many different data for this work, often data that has already been assembled for other purposes, such as administrative claims data from health plans or large national surveys.

CONFIDENTIAL

4. During the past decade, I have devoted much of my professional time to addressing the opioid epidemic. I have served as one of three Co-Editors of monographs issued by the Johns Hopkins Bloomberg School of Public Health providing comprehensive, concrete, evidence-based solutions to the epidemic. These monographs were issued in October 2015 and October 2017 (**Figure 1**); the latter report is provided as **Appendix A**. I have also testified in front of the U.S. Senate and the U.S. House of Representatives; briefed groups such as the National Governors Association, the Food and Drug Administration, Congressional Black Caucus, Centers for Medicare and Medicaid Services, and the National Academy of Science, Engineering and Medicine; and participated in efforts to improve the safe use of prescription opioids within Johns Hopkins Medicine and other health systems. My work focused on the epidemic has been funded by the Department of Health and Human Services Assistant Secretary for Planning and Evaluation (DHHS/ASPE), the Centers for Disease Control and Prevention (CDC), the Robert Wood Johnson Foundation, and the National Institutes of Health (NIH).

Figure 1. Report on the Opioid Epidemic



5. I have published extensively about opioids, including analyses of prescription opioid use in the U.S.^{2,3,4,5} as well as evaluations of the structure and impact of regulatory^{6,7,8,9,10,11,12,13,14,15,16,17,18} and payment^{19,20,21,22,23,24,25} policies on opioid prescribing, dispensing, and utilization.²⁶ I have also co-authored policy perspectives;^{27,28} a widely referenced public health review of the epidemic;²⁹ analyses of the potential impact of the coronavirus pandemic on the care of individuals with OUD;^{30,31} an evaluation of the public health impact of select abatement remedies in the U.S.;³² and the implementation of the Opioid Industry Documents Archive.³³
6. In addition to these studies, I have also led or participated in teams examining many other facets of the crisis, including: availability of naloxone in retail pharmacies;³⁴ opioid initiation among members of households with a prescription opioid user;³⁵ the effect of reformulated Oxycontin on opioid utilization;³⁶ physicians' knowledge and attitudes regarding non-medical opioid use;^{37,38} use and impact of medications for addiction treatment (MAT);^{39,40,41,42,43} the costs and healthcare utilization associated with high-risk opioid use;⁴⁴ use of automated algorithms to identify non-medical opioid use;⁴⁵ the relationship between high-risk patients receiving prescription opioids and high-volume prescribers;⁴⁶ opioid use and safety among individuals with HIV,^{47, 48, 49} chronic kidney disease,^{50,51,52,53} or recent surgery;^{54,55,56,57,58} increasing prevalence of synthetic opioids in the illicit drug supply;^{59,60} potential financial conflicts of interest among organizations opposed to the CDC's 2016 Guideline for Prescribing Opioids for Chronic Pain,^{61,62} the quality of preventive and chronic illness care received by individuals with OUD,⁶³ perceived consequences of prescription drug monitoring programs;⁶⁴ use of buprenorphine in the criminal justice system;⁶⁵ and the estimated impact of reductions in opioid prescribing on OUD and fatal overdose.⁶⁶
7. The studies I have performed examining the opioid epidemic have used a variety of epidemiologic methods, including: descriptive analyses based on cross-sectional, serial cross-sectional, and period

CONFIDENTIAL

prevalence designs; retrospective cohort studies using difference-in-difference, interrupted time-series, comparative interrupted time-series, and time-to-event designs; prospective cohort studies; qualitative assessments using grounded theory; and narrative and systematic reviews. A complete list of my publications is contained in my curriculum vitae (**Appendix B**).

8. In the first bellwether trial case in *In re: National Prescription Opiate Litigation* before Judge Dan Polster in the Northern District of Ohio, I served as an expert witness regarding how to best abate the opioid epidemic in Cuyahoga and Summit Counties. Since then, I have served as an expert witness and in some cases, provided trial and deposition testimony, in both state and federal court as outlined in **Appendix C**.
9. I received a B.A. cum laude from the University of Pennsylvania (Philosophy) in 1993, an M.D. from Case Western Reserve University in 1998, and an M.S. from the University of Chicago in 2003. A more complete description of my qualifications is found in my curriculum vitae. I performed this work through Monument Analytics, a health care consultancy that I cofounded that is separate and distinct from Johns Hopkins, and I was assisted during this process by Monument Analytics' employees and consultants. My rate of compensation for this matter is \$900 per hour. I am also reimbursed for my out-of-pocket expenses. I am not compensated based on the outcome of this matter nor the substance of my report.
10. The opinions and conclusions in this report are based on the information and documentation that was available to me at this time, and they are my own, rather than those of Johns Hopkins University. I reserve the right to supplement and revise these perspectives based on additional evidence or information that is made available to me after the date of this report.

CONFIDENTIAL

II. DATA SOURCES, METHODOLOGY, AND OPINIONS

11. In preparing this report, I reviewed materials from a number of sources, including: published reports regarding the epidemic; information derived from local and national sources; and peer-reviewed literature, whitepapers, reports from public health authorities, non-profit organizations, and other publicly available sources. Many of my findings are based on prior investigations that my team and I have either performed or synthesized, such as knowledge contained in **Appendix A** and work that I have done in other jurisdictions, such as those listed in **Appendix C**, and in citations such as references #1-#65. A complete list of the sources that I consulted in preparing this report is provided as **Appendix D**.
12. Included with my report is an appendix (**Appendix E**) that evaluates potential indicators of high-risk opioid distribution and describes their evidence base. This is important because indicators of high-risk opioid distribution are associated with an increased risk of opioid-related adverse events and death. These indicators are one important method to identify high-risk prescription opioid distribution and potential non-medical opioid use based on patterns of pharmaceutical distribution, dispensing, prescribing, or utilization.
13. I have also included an appendix (**Appendix F**) that describes the Risk Evaluation and Mitigation Strategy (REMS) program for transmucosal immediate-release fentanyls (TIRFs). Specifically, I summarize key findings from two investigations that I led regarding the impact of the REMS program on the safety and appropriateness of TIRF prescribing.^{67,68}
14. Finally, I have included an appendix (**Appendix G**) that describes the importance of preserving and providing access to opioid litigation documents for the public good. The Opioid Industry Documents Archive is an effort that is jointly sponsored by the University of California San Francisco and Johns Hopkins University. The database currently houses documents from the Mallinckrodt bankruptcy and McKinsey settlement, and is designed to house documents that may arise from future opioid litigation settlements.⁶⁹
15. In developing this report, my review of the scientific evidence base was based on a stepwise process building on the foundation of literature regarding the opioid epidemic that I was already aware of. To supplement this, I reviewed the content of additional academic and governmental studies, including both their reference lists as well as subsequent reports that have cited them. Throughout this report, I incorporate data reported by local government entities, federal agencies (e.g., Centers for Disease Control and Prevention [CDC], Substance Abuse and Mental Health Services Administration [SAMHSA], Department of Justice), community-based organizations, and peer-reviewed publications; I interpret these findings using my training and experience as well as consultation with other subject matter experts. Finally, in some instances, additional candidate articles were identified based on keyword searches of major bibliographic databases such as PubMed. In evaluating studies, I used a number of qualitative criteria that are often useful in evaluating the strength of scientific evidence supporting a given scientific finding or claim. These include factors such as the publishing journal, authorship team, affiliated institutions, funding source(s), data source(s), methodologic approach, and interpretation.^a The “Hill Criteria” (strength of association, consistency, specificity,

^a Neither these criteria nor the Hill Criteria are absolute. Rather, they serve as contextual factors that provide qualitative information that can be useful in examining the credibility of scientific claims.

CONFIDENTIAL

temporality, biological gradient, plausibility, coherence, experiment, and analogy) are also an important means of evaluating the strength of causal inference possible from a given scientific study, and I have applied these criteria as well.⁷⁰

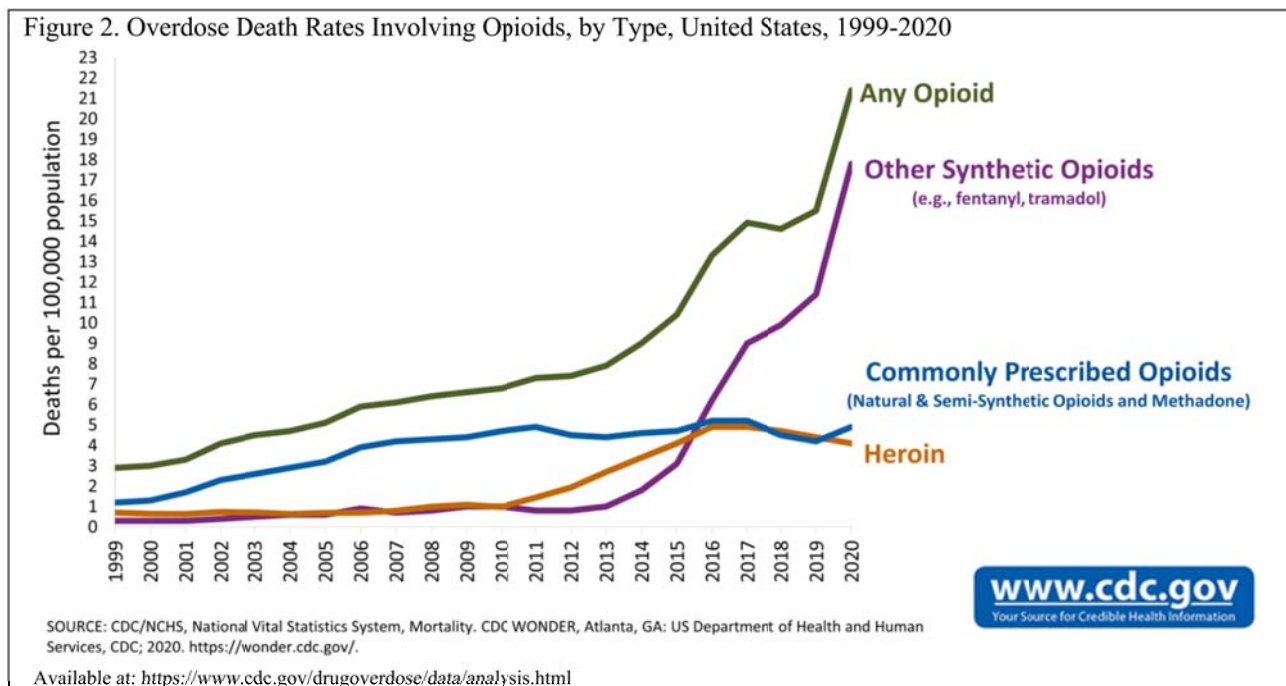
16. For some remedies to abate the opioid epidemic, such as OUD treatment or naloxone distribution and training, the evidence base is vast, with thousands of peer-reviewed manuscripts examining these matters. In these settings, formal evidence syntheses were often available, typically systematic reviews that represent a pre-specified, transparent, reproducible, highly structured approach to curating and critically appraising the totality of information required to address a carefully specified question. Because of their comprehensiveness and rigor, such evidence syntheses are often regarded as at the top of the “evidence pyramid.”⁷¹ For some abatement interventions, I also used information available from authoritative sources such as the CDC, National Institute on Drug Abuse (NIDA), or SAMHSA. Many agencies, research institutions, and organizations across the U.S. have developed analyses in an effort to abate the epidemic,^b and these serve as one of many important sources of data for my proposed plan.
17. There is widespread consensus in both public health and clinical communities that the abatement measures identified in this report are effective in reversing opioid-related morbidity and mortality. The measures discussed herein are consistent with reports forth by numerous consensus panels, task forces, professional society organizations and others. Disagreement about these solutions, when present, has tended to focus more on the priority of the interventions given limited funding (e.g., how much should be spent on law enforcement vs. medications for addiction treatment [MAT]),⁷² as well as in some cases, the potential unintended effects of some interventions. Fortunately, there is a large evidence base to guide the selection of interventions that should be undertaken in the U.S., and also a recognition of the critical point, as expressed by former Congressman John Delaney, “that the cost of doing nothing is not nothing.”⁷³
18. I conclude that an opioid epidemic persists within the United States; this epidemic continues to result in high levels of opioid-related morbidity and mortality as described in this report and in materials that I have reviewed to prepare it. I further conclude, based on my experience in epidemiology, clinical medicine, and public health, my extensive application of these fields to the opioid epidemic, and my analysis in this case, that I am able to determine what additional evidence-based and evidence-informed measures and approaches should be used to reduce opioid-related harms. These measures and approaches are described below.
19. The next sections of my report discuss the indicia of the opioid epidemic in the U.S. After that, I discuss principles that should govern an effective response, misconceptions that must be addressed, and a framework to customize abatement to local communities.

^b These include but are not limited to the RAND Corporation, the Bipartisan Policy Center, and the Pew Research Center.

CONFIDENTIAL

III. OPIOID CRISIS INDICIA AND NATIONAL ABATEMENT EFFORTS

20. Between 1999 and 2020, over 500,000 individuals in the U.S. died from an opioid overdose.⁷⁴ Since 2017, more people in the U.S. have died from opioids than from motor vehicle accidents, suicide, gun violence, or deaths at the peak of the AIDS epidemic.⁷⁵ For each year between 2015 and 2017, life expectancy in the U.S. declined, fueled in part by the epidemic.⁷⁶ Despite some progress and glimmers of hope in some communities between 2017-2019, the COVID-19 pandemic has significantly set back such efforts. The CDC recently released provisional data showing there were more than 107,000 drug overdose deaths in the United States in 2021, including 80,816 opioid overdose deaths – a 15% increase from the previous all-time high of 70,029 opioid-overdose deaths in 2020.⁷⁷
21. On the national level, the opioid epidemic has historically been characterized as having occurred in three phases.^c The first wave mirrored the increase in opioid prescribing, is characterized by a rise in prescription opioid-related deaths in the early 2000s. This was followed by a rapid increase in heroin overdose mortality beginning in 2010. The most recent transformation of the opioid epidemic is defined by the sharp increase in fentanyl overdose deaths beginning in 2016 (**Figure 2**).⁷⁸ The origins of the present-day national opioid epidemic have been well described by a variety of expert witnesses who have testified in state and federal opioid litigation, including Dr. Anna Lembke, Dr. Andrew Kolodny, and Dr. Katherine Keyes.



22. Between 1992 and 2010, the volume of opioids prescribed in the U.S. increased by approximately 400 percent.⁷⁹ Rates of addiction, overdose deaths, and many other opioid-related harms increased in

^c We and others have noted continuing changes in the nature of the overdose epidemic, and some have referred to recent increases in morbidity and mortality from cocaine, amphetamines, and mixtures of these with fentanyl as constituting a fourth wave. (Jones CM, Bekheet F, Park JN, Alexander GC. The Evolving Overdose Epidemic: Synthetic Opioids and Rising Stimulant-Related Harms. *Epidemiologic Reviews*. 2020;42:154-66.; Ciccarone D. The Rise of Illicit Fentanyls, Stimulants and the Fourth Wave of the Opioid Overdose Crisis. *Current Opinion in Psychiatry*. 2021;34:344-50)

CONFIDENTIAL

parallel.⁸⁰ The rate of opioid prescriptions dispensed peaked in 2012 at 81.3 prescriptions per 100 persons and has since declined to 43.3 per 100 persons in 2020.⁸¹ Despite this reduction nationally, significant prescription opioid morbidity and mortality persists, and there is widespread county- and state-level variation in opioid prescribing; for instance, a cluster of six states in the South^d had opioid dispensing rates greater than 64.1 per 100 persons in 2020, with Alabama having the highest rate at 80.4 per 100 persons.⁸² Additionally, there were multiple counties across the country, ranging from Virginia to Oklahoma and South Dakota with opioid dispensing rates four to nine-times higher than the national rate.⁸³

23. Fatal opioid overdoses reflect one important and tragic component of the opioid epidemic. The rate of opioid overdose deaths among individuals aged 12 years and older has increased 673% between 1999 (3.7 per 100,000 persons) and 2020 (24.9 per 100,000 persons).⁸⁴ Between 1999 and 2011, the rate of prescription opioid overdose deaths steadily increased from 1.6 per 100,000 to 6.0 per 100,000. Since 2011, the rate of prescription opioid overdose deaths has remained relatively stable while the rate of heroin and synthetic opioid deaths increased rapidly from 3.3 per 100,000 to 21.9 per 100,000. In 2020, more than 61,000 individuals lost their life to an overdose involving heroin and/or synthetic opioids, accounting for the majority of opioid overdose deaths that year.
24. As we⁸⁵ and others^{86,87,88} have argued, the COVID-19 pandemic injected new urgency into efforts to address the opioid epidemic, given that it arrived at a time when our country's response to the opioid epidemic started to coalesce. The pandemic disrupted care, including access to medications for addiction treatment, for many with OUD. Many individuals with OUD have chronic comorbid conditions which place them at higher risk from critical illness or death should they become infected, or reinfected, with COVID-19.⁸⁹ Yet a third major concern arises from the fact that addiction is “a disease of isolation”. For an already marginalized group, measures such as social distancing and quarantining pose particularly profound risks. Response efforts must continue to work to meet the needs of those impacted by the opioid epidemic, “The greatest strength of the treatment system has always been compassion and care for the most vulnerable—qualities needed now more than ever.”⁹⁰

^d Alabama, Arkansas, Kentucky, Louisiana, Mississippi, and Tennessee

CONFIDENTIAL

IV. PRINCIPLES GOVERNING EFFECTIVE RESPONSE

25. Despite the unprecedented injuries and deaths from the opioid epidemic, there is virtual consensus in the clinical, public health, and health policy communities that the epidemic can be abated. This consensus is reflected in the high concordance between a November 2017 report from the last Administration regarding the opioid epidemic,⁹¹ a report noted in Paragraph #4 that I Co-Edited and was released by the Johns Hopkins Bloomberg School of Public Health,⁹² and other groups' recommendations to prevent further harms.^{93,94,95} The Johns Hopkins report, enclosed as **Appendix A**, stemmed from three principles (**Figure 3**) that provide a valuable basis for current efforts. More recent white papers and issue briefs, such as the report released by the Office of the Assistant Secretary for Planning and Evaluation (October 2021)⁹⁶, have strong thematic alignment with these prior reports.

Figure 3. Principles Governing Johns Hopkins Report: "The Opioid Epidemic: From Evidence to Impact"

- **Informing Action with Evidence**
 - Scaling up evidence-based interventions; rapidly implementing and evaluating promising policies and programs
- **Intervening Comprehensively**
 - All along supply chain; clinic, community and addiction treatment settings; primary, secondary and tertiary prevention; creating synergies across different interventions
- **Promoting appropriate & safe opioid use**
 - Reducing overuse; focus on safe use, storage and disposal; optimizing use in accordance with best practices

26. In order to abate the epidemic, it is also important to eliminate common misconceptions about opioids and the ensuing epidemic, since inaccurate, misleading or false statements about the epidemic have allowed it to flourish. Examples of such misconceptions include:

Misconception #1: If a patient has "organic" pain, one need not worry about the addictive potential of opioids.

Reality: There is no evidence that organic pain prevents opioid addiction, and the notion that opioids are typically safe for chronic, non-cancer pain has contributed to their vast overuse.

Misconception #2: The primary driver of the epidemic is one of abuse, rather than addiction.

Reality: Abuse is a behavior and addiction is a disease; there are many lines of evidence demonstrating that addiction, rather than abuse, is the primary cause of opioid-related morbidity and mortality.

Misconception #3: The epidemic is largely driven by devious individuals such as rogue physicians and patients who are "doctor-shoppers".

Reality: Rogue physicians and "doctor-shoppers", while very important to identify and manage, account for a small proportion of opioid-related harms.

Misconception #4: If we constrain access to prescription opioids, it will just push people to heroin.

Reality: There are many factors that contribute to heroin use, and the potential for opioid policies "pushing" people to heroin underscores the need for significant treatment expansion in the United States.

Misconception #5: Non-medical use is driven by acquisition of opioids from friends or family and is separate and distinct from the oversupply arising from licensed prescribers.

Reality: Opioid oversupply from licensed prescribers is closely linked to the diversion of opioids through friends or family.

CONFIDENTIAL

V. ABATEMENT FRAMEWORK

27. There are three major categories of remedies that must be undertaken to address the opioid epidemic.^{e,f} First, we must improve the opioid prescription practices and the treatment of pain, since opioid oversupply has been a key driver of the epidemic.^{97,98} Second, we must identify and treat individuals with OUD. This is important because even if prescription opioids were to be responsibly marketed, promoted, and used beginning tomorrow, there are still millions of individuals with OUD across the U.S., many of whom require active treatment and all of whom deserve access to care if and when treatment or recovery services are sought. We must also address the large number of individuals who may have non-medical opioid use but who do not yet fulfil formal criteria for OUD. We must customize abatement remedies for specific subpopulations, including: pregnant women, new mothers, and infants; adolescents and young adults; families and children; older adults; people and communities of color; individuals experiencing homelessness or housing insecurity; and individuals with complex pain.
28. No *single* abatement remedy that is proposed can fully address the oversupply of opioids and associated morbidity and mortality in the U.S.; there are no magic bullets, and this underscores the importance of intervening comprehensively and consistently. Also, some of the abatement remedies discussed interact with one another in synergistic fashion, and successful implementation of some strategies may be dependent upon the simultaneous intervention of other strategies. For example, initiatives to decrease stigma and educate law enforcement and other community members about addiction may increase the demand for treatment, while expansions in treatment capacity to meet such demand may decrease rates of active OUD, which in turn may decrease overdose deaths and the need for naloxone. The dynamic nature of the epidemic, as well as the potential for these sorts of interactions, speaks to the vital need for surveillance and leadership as outlined in Section 1G. This will maximize the ability of communities to respond effectively to near real-time intelligence regarding key parameters of the epidemic and thus to use, and redirect, resources to maximize their public health value.
29. Some abatement approaches may be framed in the context of looking forward ten or fifteen years.^g However, the legacy of the opioid epidemic will endure far beyond that. This is because while OUD can be treated and may remit, it is not curable, and some individuals with OUD will require treatment indefinitely.^{99,100,101} Others have acquired HIV and/or HCV as a result of an addiction that began with prescription opioids,^{102,103} and they may require indefinite care for these comorbid conditions. Foster care for those orphaned by the epidemic, child protective services, and services for children impacted by opioid use in utero must be resourced to address the needs of children and young adults as they grow and develop. Opioid use and its sequela also contribute to intergenerational trauma that may perpetuate over time. For many, living healthy, productive lives in recovery is an active process, and

^e Other interventions are important in addressing the epidemic yet beyond the scope of this report, such as changes to coverage and reimbursement policies so as to improve options for pain treatment and reduce financial barriers to OUD treatment.

^f While there are other ways to classify potential remedies, the elements within these remedies are remarkably consistent across different abatement proposals put forth locally and nationally, reflecting the widespread consensus about what needs to be done.

^g This medium-term view strikes a balance – it is long enough to support infrastructure development and several cycles of planning and evaluation while avoiding some of the uncertainty entailed in trying to anticipate the magnitude of sequelae from the epidemic that may last decades or even generations.

CONFIDENTIAL

thus to be successful, individuals must be supported with long-term resources to maximize their opportunities for success.

30. For each of the categories below, in the following sections of my report, I provide background and scientific context, components of abatement interventions corresponding to each category, and concluding thoughts.

Category 1: Prevention - Reducing Opioid Oversupply and Improving Safe Opioid Use

- 1A. Health Professional Education
- 1B. Patient and Public Education
- 1C. Safe Storage and Drug Disposal
- 1D. Harm Reduction
- 1E. Prescription Drug Monitoring Programs
- 1F. Community Prevention and Resiliency
- 1G. Leadership, Surveillance, and Implementation

Category 2: Treatment - Supporting Individuals Affected by the Epidemic

- 2A. Connecting Individuals to Care
- 2B. Treatment for Opioid Use Disorder (OUD)
- 2C. Addressing Non-Medical Opioid Use
- 2D. Managing Complications Attributable to the Epidemic
- 2E. Workforce Expansion and Resiliency
- 2F. Distributing Naloxone and Providing Training

Category 3: Recovery - Enhancing Public Safety and Reintegration

- 3A. Public Safety
- 3B. Criminal Justice System
- 3C. Vocational Training
- 3D. Mental Health and Grief Support

Category 4: Addressing Needs of Special Populations

- 4A. Pregnant Women, New Mothers, and Infants
- 4B. Adolescents and Young Adults
- 4C. Families and Children
- 4D. Older Adults
- 4E. Black, Indigenous, and People of Color (BIPOC)
- 4F. Individuals Experiencing Homelessness and Housing Insecurity
- 4G. Individuals with Complex Pain

CONFIDENTIAL

CATEGORY 1: PREVENTION – REDUCING OPIOID OVERSUPPLY AND IMPROVING SAFE OPIOID USE

The purpose of this category is to further reduce the oversupply of opioids, promote public education and awareness, and support efforts to evaluate and respond to the epidemic across the U.S. so as to decrease injuries and deaths from opioids.^h This category is vital to reducing harms from the opioid epidemic because the oversupply of prescription opioids during the past two decades has been an important driver of the epidemic.ⁱ Harm from this oversupply arises from many points in the continuum of care, ranging from how clinicians treat pain to the diversion of opioids throughout the supply chain.

A. HEALTH PROFESSIONAL EDUCATION

The goal of this remedy is to train health care providers, including prescribers and other health care personnel, such as dispensers (pharmacists) and emergency medical technicians (EMTs), regarding the appropriate use of opioids in clinical practice, as well as how to identify and appropriately respond to patients who may have OUD. This is important because historically, many providers have overestimated the effectiveness of opioids and/or underestimated their risks. This has contributed to the oversupply of opioids, not only with respect to whether they are used at all, but also with respect to the dose and duration of use. In addition, OUD is often not recognized in clinical practice, and even when recognized, the delivery of treatment and recovery services often falls short.

31. One of the most systematic and well-studied approaches to direct training of prescribers, sometimes referred to as “academic detailing”, should also be employed. Academic detailing is a method of evidence-based, interactive outreach to prescribers that uses trained personnel to make face-to-face visits with clinicians to promote optimal prescribing and improve the quality of patient care. Established in the 1980’s, there are dozens of studies that provide evidence of its value,^{104,105,106,107} including an investigation indicating large decreases in opioid prescribing following a multi-level intervention that included academic detailing.¹⁰⁸ A systematic review of the impact of provider education, the most comprehensive assessment of its kind, concluded that this strategy results in significant improvements in prescribing quality,¹⁰⁹ and this narrative is consistent with a large literature overview examining the effectiveness of interventions to shape prescriber behavior.¹¹⁰
32. In addition to the numerous studies summarizing the evidence base for academic detailing outlined above, some studies have also examined the potential impact of such education on opioid-related measures. A multi-modal intervention between 2010 and 2015 using surveillance, academic detailing, and clinical decision support tools within Kaiser Permanente Southern California was associated with a 30% reduction of high-dose opioids, a 98% reduction in large quantity (i.e., over 200 pills) opioid dispensing, and a 72% reduction of long-acting and extended-release opioids among 3.2 million adults in the Kaiser Permanente Southern California system.¹¹¹ Similarly, a quality improvement study comparing a six-month pre-intervention baseline with a 16-month post-intervention period ending in April 2018 at a regional health system in Maryland documented a nearly 40% decrease in the overall opioid prescription rate, a 60% decrease in the quantity of opioids prescribed per visit, and a reduction in the strength of opioids prescribed following a public and provider education

^h This category excludes consideration of Drug Enforcement Agency (DEA) quotas, controlled substance scheduling and other mechanisms the federal government may use to reduce supply of opioids or precursors in the marketplace.

ⁱ Reductions in opioid oversupply will also decrease opioid demand, since opioids are highly habit forming, tolerance quickly develops and a substantial minority of individuals receiving chronic opioids develop OUD.

CONFIDENTIAL

campaign.¹¹² Patient satisfaction surrounding pain management in the emergency department also improved.

33. Academic detailing has also been used to increase naloxone use.^{113,114} An analysis of Veterans Affairs (VA) facilities between 2014 and 2017 found that facilities that received academic detailing had a rate of naloxone prescribing that was five-times higher than their counterparts.¹¹⁵ Of the estimated increase of 15,000 naloxone prescriptions among facilities receiving academic detailing, two-thirds went to patients at a high risk of overdose due to the quantity or type of opioids prescribed. Another study of 40 primary care providers in San Francisco found that those receiving detailing had a ten-fold higher rate of prescribing naloxone than their counterparts;¹¹⁶ physician participants reported that because of the educational outreach, they were able to open new conversations with patients to promote safer and more compassionate care.
34. Efforts to reduce the oversupply of opioids should be coupled with information regarding the principles of sound pain management, including through a focus on comprehensive assessments, multidisciplinary management, and functioning rather than pain levels per se. Opioids represent just one of a large number of pharmacologic and non-pharmacologic treatments that providers and patients may use for the treatment of pain. Alternative pharmacologic treatments include acetaminophen, non-steroidal anti-inflammatories (NSAIDs), antidepressants, anticonvulsants, and topical analgesics;¹¹⁷ while non-pharmacologic treatments for pain include increasing physical activity or exercise, physical therapy, occupational therapy, chiropractic care, and psychological interventions.¹¹⁸ In addition, the care of pain among those already engaged in non-medical opioid use or with OUD requires additional skill and training given the need for clinical management of both.
35. Training on the management of patients who have been maintained on chronic opioids is also important, especially the subset of patients on high-dose opioids (e.g., greater than 90 morphine milligram equivalents per day). Since patients using opioids chronically are physically dependent on them,^j they must not have their opioids abruptly discontinued, nor should tapering be performed unilaterally. An increasing number of guidelines for tapering opioids among these individuals are available.^{119,120} These guidelines include information on when tapering should be considered among patients on long-term opioid treatment, which often occurs when adverse effects or the risk of adverse effects (e.g., sedation, drowsiness, constipation, nausea) outweigh potential benefits with respect to reductions in pain and improvements in physical, psychological and/or social functioning.¹²¹ The guidelines also speak to the optimal management of individuals who, based on taper failure, may fulfil criteria for persistent opioid dependence and who may be best managed through long-term opioid treatment, such as buprenorphine or methadone. In fact, a systematic review found that transitioning patients who received long-term opioid therapy to buprenorphine did not precipitate opioid withdrawal and reduced chronic pain intensity.¹²²
36. While there are many criteria that could be used to select physicians who should receive academic detailing, a conservative approach would be to focus on approximately 10% of all active, ambulatory

^j Within a few weeks or less, all patients using opioids develop physical dependence, a predictable neurochemical change associated with sustained use. By contrast, addiction is far less predictable, represents compulsive use despite harm, and is often associated with impairment in social, psychological and/or physical functioning.

CONFIDENTIAL

patient-care prescribers – those that account for the highest prescribed opioid volume.^k Because opioid prescribing is highly skewed, such a focus, properly designed, could reach prescribers accounting for the majority of opioids in the marketplace. For example, we previously found that fewer than 5% of prescribers in Florida accounted for approximately two-fifths of opioid prescriptions and two-thirds of opioid volume during a given calendar year.¹²³ Similarly, a study of workers compensation claims in California indicated that approximately 87% of opioid volume was accounted for by the top 10% of prescribers.¹²⁴

37. Since academic detailing should target high volume prescribers in communities across the U.S., it must be based on information regarding specific individuals' prescribing behaviors. One source of such information would be prescription drug monitoring programs (PDMPs). An alternative source of similar data would be from a market intelligence firm, such as Symphony Health or IQVIA. These companies license data regarding prescription drug prescribing to pharmaceutical companies and other clients, and may represent a source of more efficiently gathered, possibly better curated and more timely information regarding both physician and non-physician prescribers (e.g., advanced nurse practitioners, physicians' assistants).¹²⁵
38. The value of provider education lies in the quality of the information that is delivered. Thus, the information must be of the highest quality and from the most reputable sources. A natural foundation for this effort would be the 2022 Centers for Disease Control and Prevention (CDC) Guideline for Prescribing Opioids, given the credibility of the CDC, the extraordinary rigor that was exercised in its development.^{126, 127, 1} Building on the 2016 Guideline, the 2022 Guideline delineates recommendations for patients with acute and subacute pain. This Guideline can be cross-referenced with other scientifically rigorous guidelines and sources used by established provider education programs so long as they are suitably protected from undue commercial influence.¹²⁸ In addition to delivering information about best practices, academic detailing should also include reports on prescribing patterns and metrics so that individual prescribers or dispensing pharmacists can review and critically evaluate their own prescribing or dispensing patterns relative to peers at local, regional, and national levels, as well as to identify instances of prescribing or dispensing that may warrant closer and more critical evaluation. A recent randomized trial found a significant reduction in the number of prescription opioid pills and MMEs per opioid prescription for prescribers who received monthly feedback on how their opioid prescribing compared to that of other prescribers.¹²⁹
39. Provider education has to deliver a limited number of focused messages or it will not be effective. The draft 2022 CDC Guideline for Prescribing Opioids includes twelve scientifically supported "clinical reminders" that can be used as a basis for provider education modules:
 - 1) Non-opioid therapies are effective for many common types of acute pain;
 - 2) Non-opioid therapies are preferred for subacute and chronic pain;
 - 3) Use immediate-release opioids when starting opioid therapy;

^k While this discussion focuses on ambulatory care, an increasing number of evidence-based guidelines are also available for the post-surgical setting, where opioids have also been heavily oversupplied; an academic detailing program should also be considered for these prescribers as well.

¹ While the CDC Guideline for Prescribing Opioids and Chronic Pain is one of the most comprehensive, authoritative, and widely cited opioid guidelines, any academic detailing program as part of an abatement remedy should be based on an assessment of the most current and suitable sources of information for such a program.

CONFIDENTIAL

- 4) For opioid-naïve patients, clinicians should first prescribe the lowest dosage to achieve expected effects;
 - 5) For patients already receiving higher opioid dosages, clinicians should carefully weigh benefits and risks and exercise care when reducing or continuing opioid dosage;
 - 6) When treating acute pain, prescribe quantities no greater than what is needed for the expected duration of pain that is severe enough to warrant opioids;
 - 7) Clinicians should evaluate benefits and risks with patients within 1 to 4 weeks of starting opioid therapy;
 - 8) Discuss benefits and risks, as well as the availability of non-opioid therapies with patients;
 - 9) Utilize the PMP data to determine whether a patient is receiving other therapies that put them at risk;
 - 10) Urine drug testing should be utilized to assess for the presence of other medications and illicit substances;
 - 11) Avoid concurrent benzodiazepine and opioid treatment; and
 - 12) Arrange treatment for patients with opioid use disorders.¹³⁰
40. The draft 2022 CDC Guideline improve upon clinical guidelines that emerged from the liberalization period in the 1990s in several important ways. For example, in 1997, the American Academy of Pain Medicine and the American Pain Society issued a consensus statement that endorsed the use of opioids to treat chronic, non-cancer pain, arguing that “studies indicate that the de novo development of addiction when opioids are used for the relief of pain is low.”¹³¹ By contrast, the 2022 CDC Guideline underscore the risks of addiction and other adverse events related to prescription opioids, recommends lower dosages, focuses on improving safe use among all, rather than “high-risk”, patients, and provides more specific guidance regarding how to best monitor opioid use and establish thresholds for stopping them in the setting of unfavorable risks/benefit balance.¹³²
41. The National Resource Center for Academic Detailing (NaRCAD), a center aimed to support clinical outreach education programs, provides an extensive directory of established provider education programs, including a section for those dedicated to opioid safety.¹³³ For example, Alosa Health is a non-profit that has deep experience in this area conducting state and nationwide campaigns.^{134,135} While pharmaceutical companies and pharmacy benefit managers (PBMs) both have extensive workforces available for direct prescriber outreach, neither would be credible in this setting given the conflicts of interest that would be posed. Instead, provider education programs typically recruit physicians, nurses, pharmacists or other individuals with a background in related health disciplines to conduct outreach.
42. Regardless of the detailer’s background, it is essential that educators have no potential commercial conflicts of interest, have a background in a health discipline such as medicine or pharmacy, and receive rigorous training on how to conduct this outreach. Lack of clinical knowledge may cripple the detailer’s credibility with the prescriber, making it difficult to establish a strong relationship that promotes rational prescribing. Furthermore, it is also important that the outreach is repeated over time, with follow-up visits to encourage positive changes and reinforce key messages.

CONFIDENTIAL

43. In addition to academic detailing of prescribers, broader health professional education should also be considered for at least four types of health care providers:
- Licensed prescribers (beyond those selected for academic detailing based on high opioid prescribing), such as physicians, dentists, nurse practitioners, and physicians' assistants, are important to target because they issue prescriptions for opioids and other analgesics.
 - Nurses, especially in settings such as Emergency Departments, urgent care, and other clinical areas where opioids are commonly used, should be targeted because they are in an influential position to shape the culture of pain management and to raise awareness about evidence-based methods to identify and treat pain and OUD.
 - Dispensers, or pharmacists, should be targeted because they dispense opioids and are increasingly responsible for implementing drug utilization management policies and practices designed by payers and PBMs. Furthermore, pharmacies are obligated to exercise their "corresponding responsibility" to insure that opioid prescriptions are not filled unless there is a legitimate medical purpose".¹³⁶
 - Emergency medical technicians (EMTs) are important to reach because they are often the first point of contact with individuals who have overdosed, and thus in a key position to bridge a common treatment gap that contributes to low rates of evidence-based treatment for OUD, namely, individuals who are resuscitated but not connected with OUD treatment.
44. Resources permitting, education of other health care personnel, such as pharmacy technicians and physical therapists, should also be undertaken. Since opioid oversupply, as well as OUD, are both so common, these personnel also regularly engage with patients who have a high likelihood of being harmed by the epidemic, and thus they too are in a position to support a required cultural shift in the paradigm of pain and OUD identification and management in the U.S.
45. In addition, while training and professional development of health care personnel such as doctors, nurses and EMTs is vital, additional educational capacity-building and technical assistance must be employed if the opioid epidemic is to be successfully addressed. For example, hospitals, health systems, integrated delivery networks, physician practices, long-term care facilities, and other health care institutions and organizations should work diligently to incorporate educational programming and professional development services that assist in raising awareness and disseminating knowledge regarding the drivers of the opioid epidemic, as well as the role of their respective institutions in addressing it. In some instances, such programming may be delivered through Continuing Medical Education (CME), Continuing Nursing Education (CNE), or similar vehicles, although it is important that any such programming be scrupulously developed and monitored to minimize the potential for bias that might jeopardize the quality and impact of such materials.¹³⁷ Health systems play an especially important role given their broad reach and ability to promulgate evidence-based guidelines, as well as to engage in opioid stewardship.¹³⁸ Technical assistance to the courts, law enforcement, substance use treatment providers, and other stakeholders should also be provided so as to ensure that these entities are kept abreast of the changing contours of the epidemic and the most relevant advances in prevention, treatment, and recovery.
46. In conclusion, abatement programs in the U.S. should include health professional education. Efforts such as academic detailing are feasible and can be highly scaled as well; numerous state-wide and even national provider education programs promoting safe prescribing have been conducted during the past two decades, including across Pennsylvania (e.g., Department of Aging Pharmaceutical

CONFIDENTIAL

Assistance Contract for the Elderly [PACE] Academic Detailing Program),¹³⁹ Massachusetts (e.g., Boston Medical Center's Transforming Opioid Prescribing in Primary Care),¹⁴⁰ and the United States Department of Veterans Affairs (e.g., National Academic Detailing Service).¹⁴¹ Many health systems, including large integrated delivery networks such as Kaiser Permanente,¹⁴² have also executed such programs. Careful review of the evidence indicates that academic detailing works and that it would be an effective abatement tool for communities,¹⁴³ and it should be combined with broader health professional education as discussed above.

CONFIDENTIAL

B. PATIENT AND PUBLIC EDUCATION

The goal of this remedy is to raise awareness and activate patients and the general public regarding the risks of opioids as well as the prevalence and treatability of OUD. Patient and public education can help to address the fact that many people do not understand the risks of opioids or that OUD is a treatable brain disease. It can also help to reduce stigma, which serves as a profound barrier to treatment.

47. Patient education is an important method of improving the safe use, storage, and disposal of opioids, since there are important shortcomings in patients' knowledge regarding these matters. For example, the draft 2022 CDC Guideline highlights the importance of clinicians discussing with patients the known risks and realistic benefits of opioid therapy before initiating treatment.¹⁴⁴ Other professional societies and organizations, such as the Veterans Administration/Department of Defense Clinical Practice Guideline for Opioid Therapy for Chronic Pain, also emphasize the importance of patient education as part of a multi-faceted strategy to maximize the risk/benefit value of opioids in clinical practice.¹⁴⁵
48. In contrast to public education, which is addressed below, clinicians play an especially important role in educational outreach targeting patients who may be using opioids or otherwise at risk for opioid-related adverse events. However, clinicians themselves must be equipped to conduct such education, and their preparation for this can be maximized through academic detailing or other educational outreach as previously described. Educational materials have been developed by the CDC to promote safer opioid use and minimizing the risk of overdose;¹⁴⁶ SAMHSA's Opioid Overdose Prevention Toolkit includes a module providing safety advice for patients and family members;¹⁴⁷ and other organizations, such as the American College of Surgeons,¹⁴⁸ have developed their own messaging that can be used to educate patients regarding different aspects of the opioid epidemic.
49. Public education is also a crucial component in abating the epidemic, and one important way to conduct such education is through tailored mass media campaigns.^m When properly designed and branded, such campaigns can deliver "sticky" messages, that is, messages that are concrete, memorable, contagious and therefore, impactful.¹⁴⁹ Such messaging can serve as part of an effective intervention to positively change health behavior.^{150,151} Despite this, not all mass media campaigns have been successful in achieving their desired impact,¹⁵² and their success is dependent on several factors including the level and duration of investment made, the planning that goes into the campaign, and the availability of concurrent treatment and other services. A mass media campaign may include a variety of media, including television, radio, billboards, and social media. Though there is limited literature on mass media campaigns focusing on opioids, there is robust information from campaigns on alcohol, tobacco, and other illicit substances.
50. A number of these campaigns can be used as models when designing campaigns to address the opioid epidemic. For example, Idaho's Meth Project was aimed at reducing methamphetamine use through a comprehensive approach of public service announcements, community outreach, public policy approaches, and in-school lessons. Following the campaign's initiation in 2007, Idaho experienced a 56% decline in meth use amongst teens.¹⁵³ The U.S. Food and Drug Administration's (FDA) award-winning youth tobacco prevention campaign, "The Real Cost", is another example of a relatively

^m Faith-based communities are another important method of public outreach, given their potential to reach large numbers of individuals and the trusted role that faith-based leaders play in many individuals' lives.

CONFIDENTIAL

recent mass media campaign. This campaign was launched nationally on multiple platforms, including TV, radio, print, and social media. The campaign was focused on reaching youths, 12 to 17 years old in the U.S., who were open to trying smoking or were already experimenting with smoking. In 2014-2016, high exposure to the campaign was associated with a 30% decrease in the risk of smoking initiation amongst youths.¹⁵⁴ Also, Florida's Bureau of Tobacco Free Florida has aired the Tobacco Free Florida campaign since December 2010.¹⁵⁵ The campaign used evidence-based advertisements with strong emotional content and graphic imagery. A study that examined data from 5,418 adult cigarette smokers and recent quitters between 2011 and 2018 found that exposure to the campaign was associated with increased odds of a quit attempt in the previous 12 months.

51. Several mass media campaigns addressing the opioid epidemic have been conducted nationwide.^{156,157} For example, in January 2017, then New Jersey Governor Chris Christie rolled out the ReachNJ initiative aimed at raising awareness about the availability of new addiction treatment services in New Jersey.¹⁵⁸ The initiative included television ads airing on New Jersey, New York, and Philadelphia television stations. As of January 2018, more than 18,600 people had called the ReachNJ hotline, with the frequency of calls at least three-times higher in April-June 2017, when television and radio ads were on air, compared to July-August, when only digital ads were used.¹⁵⁹ A second, 2017 CDC-funded program used video advertisements, radio advertisements, digital materials, and print materials to increase awareness and knowledge about the risks of prescription opioids.¹⁶⁰ Piloted in Ohio, Oregon, Rhode Island, and West Virginia, over 70% of individuals exposed to campaign materials correctly identified the campaign's message of preventing non-medical use of pain medications and over 50% linked this to the goal of preventing overdose deaths.
52. An additional example of a mass media campaign was designed to raise awareness about a new law increasing naloxone access and providing legal protection for people who call 911 to report an overdose. This state-wide media campaign in North Carolina focused on leveraging inexpensive platforms such as social media, printed flyers, public service announcements, and local media and was reported as effective in building connections with the local community and helping the organization become established as "the go-to expert for local media" regarding the epidemic.¹⁶¹ Additionally, "The Truth About Opioids" was a mass media public education campaign Rhode Island targeted at young adults that delivered messages through television and digital media with the aim of preventing opioid misuse and dependence.¹⁶² A study of 1,434 young adults surveyed before and after the campaign was aired found that awareness of the campaign was associated with greater campaign-targeted opioid-related knowledge, decreased levels of stigma, and an increased likelihood to talk to a friend about the opioid epidemic.
53. In conclusion, abatement initiatives should include investments in educational campaigns targeting patients and the general public. Multimedia campaigns should include experts in health communications and public safety and be carefully designed to fully address widely prevalent yet insidious stigma that erodes effective community responses to the epidemic, treating addiction as a willful choice or moral failure, and cleaving off addiction and its treatment from other health care.¹⁶³ These campaigns must also educate the general public both about the risks of opioids as well as the prevalence of OUD and its responsiveness to treatment. In addition, they should include messaging around the safe storage and disposal of opioids, since many individuals receiving opioids do not report having received such information.¹⁶⁴

CONFIDENTIAL

C. SAFE STORAGE AND DRUG DISPOSAL

This remedy respects the principle of intervening comprehensively along the prescription opioid supply chain, including addressing enormous stockpiles of opioids in homes across the U.S., by providing individuals with convenient opportunities to safely store and discard unused medicines.

54. Safe storage and drug disposal guidelines are a critical component of public education since the improper storage and disposal of unused prescription opioids is a widely recognized public health concern and an important component of the current opioid epidemic. Our own work suggests an increased risk of opioid initiation among household members of those prescribed opioids¹⁶⁵ – including an increased risk of opioid overdose among adolescents and young adults.¹⁶⁶ In a 2017 systematic review that my colleagues and I published in JAMA Surgery, 67-92% of surgical patients reported having unused opioids after surgery, and in two studies examining storage safety, 73-77% of patients did not store their opioids in locked containers, resulting in a large reservoir of opioids which contributes to the non-medical use of these products.¹⁶⁷ Other studies also support the assertion that the safe storage and proper disposal of opioids is uncommon.¹⁶⁸ The failure to safely store and dispose of unused opioids extends beyond surgical settings and contributes to the diversion of opioids as well as their non-medical use.¹⁶⁹ For example, of the 11.4 million individuals in the U.S. reporting non-medical opioid use in 2017, more than four in five (83%) reported that they bought, were given, or stole opioids from individuals who were in turn prescribed these drugs by a licensed prescriber.¹⁷⁰
55. Safe storage and drug disposal guidelines must be accompanied by increased availability of drug disposal programs, since these programs provide one avenue for proper disposal of unused opioids.¹⁷¹ Some disposal programs are based on periodic events. For example, the U.S. Drug Enforcement Administration (DEA) hosts short-term events wherein temporary collection sites are set up for the safe disposal of unused prescription medicines. Held on September 25, 2010, the DEA conducted the first-ever national drug take-back day, collecting over 121 tons of medications at more than 4,000 sites nationwide.¹⁷² The DEA's National Take Back Day on October 23, 2021 included the participation of 4,276 law enforcement personnel and 4,982 collection sites collecting a total of 372 tons of prescription drugs.¹⁷³ Other disposal programs are based on permanent collection sites authorized by the DEA, such as within pharmacies or law enforcement facilities.
56. Unless disposal programs are convenient, they are unlikely to be widely used, and the use of pharmacies as part of a “reverse logistics” program, where the standard distribution system is reversed to return unused or unwanted product, has many efficiencies.¹⁷⁴ Some authorized collection sites may also provide mail-back options to assist patients in disposing unused medicines, especially for homebound patients or others with special needs. Local pharmacies may also provide free deactivation packets that individuals can use to deactivate their unused controlled substances before discarding them in the trash.
57. Although patients may favorably perceive drug disposal programs,¹⁷⁵ historically, permanent collection sites have been uncommon due to administrative, legal, and economic barriers. As of 2017, the United States Government Accountability Office reported that only 2,233 of 89,550 eligible entities (2.5%), such as pharmacies, hospitals/clinics, narcotic treatment programs, reverse distributors, distributors, and manufacturers, were registered as authorized collectors of unused prescription drugs.¹⁷⁶

CONFIDENTIAL

58. Despite their importance, historically, drug disposal programs have only re-collected a small proportion of the total number of controlled substances dispensed, with collected drugs also including a mix of other medications such as antibiotics, oral contraceptives, and cardiovascular treatments.¹⁷⁷ Furthermore, the U.S. FDA directs that certain prescription medicines, such as opioids, should be immediately flushed down the toilet when no drug disposal program option is readily accessible.¹⁷⁸ Other routes of disposal include mixing unused opioids with inedible garbage (e.g., cat litter) or using specialized chemicals that trap the unused pills in a non-divertible and biodegradable matrix.¹⁷⁹ In addition to expanding drug disposal programs, patient and pharmacist education regarding how to properly dispose of opioids is also vital.
59. The implementation of drug disposal programs will vary across communities. For example, staffing needs will vary based on the magnitude of work involved. There are four major components to consider when establishing and maintaining a drug disposal program: (1) promotion; (2) staffing; (3) equipment and supplies; and (4) disposal.^{180,181} Equipment, supplies, and frequency of disposal will depend upon the volume of drugs collected, which can be estimated based on the local population. For context, prior studies of drug-take back initiatives based in pharmacies and police departments in rural counties report approximately 600 pounds of medications are collected a year.^{182,183}
60. In conclusion, abatement programs should include investments to educate individuals regarding safe opioid storage and disposal, as well as to expand the availability and convenience of drug disposal programs. While periodic “take-back” days, such as those coordinated with the DEA, are impactful, such episodic programs should be complemented by accessible permanent collection sites that are continuously operated. In addition to placing take back kiosks within Police Departments, programs should be implemented throughout community pharmacies as well as urgent care centers, hospitals and health systems. For select populations, such as homebound elderly or others with special needs, it may also be helpful to invest in mail-back options and/or the distribution of biodegradable technologies that allow for safe and convenient at-home disposal.

CONFIDENTIAL

D. HARM REDUCTION

The goal of harm reduction is to implement evidence-based interventions that “meet people where they are at”, as compared to zero-tolerance approaches that criminalize opioid use, propagate stigma, and serve as a barrier to accessing treatment. Such approaches recognize the formidable barriers that often prevent people from seeking treatment or achieving full recovery; harm reduction will decrease individual and societal harms from the opioid epidemic in the U.S.

61. Harm reduction refers both to a set of general principles used to underpin policies concerning the way that societies respond to drug problems and to specific interventions. A defining feature of these approaches is their focus on harms associated with opioid use rather than the prevention of such use per se. Harm reduction approaches can target individuals as well as the structural (e.g., drug paraphernalia laws)¹⁸⁴ and environmental (e.g., physical environment) contexts which engender harm. In addition to providing preventive services that reduce the burden of disease, such as skin and soft tissue infections, HIV, HCV, and chronic diseases, and offering a source for individuals to be linked to treatment, harm reduction programs can also reduce stigma by providing education to the community.¹⁸⁵ It is important to note that there is no evidence to support the notion that harm reduction services encourage and enable drug use.¹⁸⁶
62. Harm reduction can be contrasted with approaches that prioritize only prevention of drug use, which often are embodied in “zero tolerance” enforcement approaches.¹⁸⁷ Empirical evidence has demonstrated short-comings of the U.S. “War on Drugs”,^{188,189} including its failure to reduce the demand for drugs^{190,191} or decrease drug-associated violence¹⁹² while leading to the disproportionate incarceration of people of color and the urban poor. Such findings underscore the need for innovative, evidence-based approaches to address OUD and other harms stemming from non-medical opioid use. An important component of any comprehensive response to the opioid epidemic includes scaled-up harm reduction services targeting people who are actively using drugs. There are four main harm reduction approaches that are relevant to the opioid epidemic and discussed below: syringe services programs, overdose prevention sites, drug sobering centers, and drug checking services. Naloxone is discussed separately in Section 2F of this report.
63. Syringe services programs (SSPs) are designed to provide clean syringe access and disposal to people who inject drugs (PWID). Such programs were scaled up in the U.S., Europe, and Australia in the 1990’s and 2000’s to help reduce the transmission of blood-borne infectious diseases as discussed in Section 2D below. The U.S. Public Health Service has long recommended to have a clean syringe for every injection, effectively increasing the “coverage” of sterile injection equipment.¹⁹³ Through extensive research over three decades, SSPs have been associated with reductions in risky syringe sharing behaviors,^{194,195,196} as well as rates of HIV,^{197,198,199,200} hepatitis B, and HCV.²⁰¹ A study by the National Institutes of Health found that syringe exchange programs are associated with a reduction in risk behaviors as high as 80% among injection drug users.²⁰² A systematic review of SSP studies, including many from the U.S., found that SSPs are associated with a 32% reduction in the transmission of HIV and approximately a 50% reduction in HCV incidence among PWID.²⁰³
64. Syringe service programs also reduce the financial burden to communities by preventing disease transmission, decreasing overdose and injury associated with drug use, and increasing the likelihood of linking individuals with substance use disorder treatment.^{204,205} This is because SSPs generally include onsite evaluation and referrals for substance use disorder treatment for an otherwise difficult

CONFIDENTIAL

to access population. As of April 2021, there were 354 SSPs in 42 U.S. states and Washington, D.C.²⁰⁶ Despite anecdotes to the contrary,²⁰⁷ SSPs do not increase illegal drug use or crime. For example, analyses of such programs in New York City and Baltimore indicate no difference in crime rates between areas with and areas without SSPs, including trends in arrests and violent crimes.^{208,209}

65. Syringe service programs often provide medical services for PWID, many of whom are marginalized and may have otherwise very limited access to ambulatory care. In addition to doctors, nurses, and social workers, such care may include peer support specialists, whose potential value and services are discussed in Section 2A. Clinical services delivered as part of SSPs may include care for acute conditions such as upper respiratory infections, chronic conditions such as diabetes or cardiovascular diseases, or most commonly, preventive screening and other preventive interventions such as flu shots or other vaccinations. Such programs may also include family planning services. Individuals who test positive for HIV, HCV, or both should be referred for treatment. Positively identified individuals will require access to necessary health care, including effective antiretrovirals and direct-acting antiviral treatments that treat HIV and HCV, respectively, as well as treatment for their underlying OUD, including access to MAT and other treatments for opioid use disorder.
66. Syringe service programs can be implemented as stationary walk-in programs or as mobile units. Mobile harm reduction programs are one tool to significantly improve access for hard-to-reach populations, including those that do not have access to transportation or who may reside in rural areas. A review of twelve HIV Outreach programs which included harm reduction services found that clients who accessed mobile units were 86-times more likely to receive an HIV test than those who accessed other sites.²¹⁰ The authors noted that mobile outreach increased recognition and opportunities to initiate conversations with new clients and such outreach may increase the likelihood that an individual will enter treatment.
67. Overdose prevention sites, sometimes called supervised consumption sites, are places where people can consume previously purchased opioids under medical supervision where staff can promptly respond to individuals who experience an overdose. In the past 30 years, at least 100 overdose prevention sites have been established across Canada, Europe, and Australia, with evidence to date suggesting that they prevent overdose death, reduce transmission of infections and public drug use.^{211,212,213,214,215} These sites are primarily staffed by nurses and case managers who do not assist in drug administration²¹⁶ and are equipped to address questions about how to decrease the risks of drug consumption, provide sterile equipment (e.g., syringes), and reverse an overdose.
68. In addition to their public health impact and cost-effectiveness,²¹⁷ overdose prevention sites are uniquely effective in sustaining contact with the most marginalized PWID^{218,219,220} and positively impact communities by reducing public drug use.²²¹ In January 2021, the Institute for Clinical and Economic Review (ICER) published a comprehensive evaluation of overdose prevention sites, finding they:²²² (1) prevent overdose deaths instead of delaying them; (2) reduce or prevent expenditures on emergency room visits, hospitalizations, and EMS calls; (3) do not affect crime rates; (4) may decrease public drug consumption and injection litter. Several communities across the U.S. have opened, or are in the process of opening, sanctioned overdose prevention sites.²²³ However, despite substantial evidence of their public health benefit, there are legal and political challenges to establishing these sites in many communities.

CONFIDENTIAL

69. Drug checking services enable people who use drugs to have the content of their drugs chemically analyzed, allowing them to make informed decisions about use.^{224,225} Drug checking, a method pioneered in Europe, has the potential to introduce the concept of product safety into the unregulated illicit drug supply in the U.S. Currently, its use in the U.S. has been limited primarily to testing for 3,4-methylenedioxy-methamphetamine (MDMA, or “ecstasy”) at large dance parties. Recently, some U.S. SSPs have begun distributing fentanyl testing strips originally designed for testing urine samples.²²⁶ Such “fentanyl checking” allows users to objectively determine whether their drug samples contain fentanyl or fentanyl analogues. Though some may argue that the widespread prevalence of fentanyl decreases the utility of drug checking machines or fentanyl testing strips, there remain key reasons to support testing: (1) drug supply and composition is not consistent over time and circumstances may change in various communities; (2) testing serves as a reminder for intravenous drug use hygiene, including acquiring extra doses of naloxone or consuming drugs with a friend present; and (3) it can identify counterfeit pills. This is important in part because the drug market is unstable and prone to dramatic fluctuations in product composition.^{227,228} As such, drug checking machines allow individuals to check for other cutting agents, such as benzodiazepines, that increase the risk of injury or death.
70. While few evaluations of fentanyl testing services have been performed, assessments suggest a high degree of acceptability and potential utility among PWID,^{229,230,231} and early evidence suggests checking for fentanyl in drug samples at SSPs, police departments, and other relevant sites may help guide appropriate responses to the changing nature of the opioid epidemic. For example, a study conducted in Greensboro, North Carolina, found that 43% of people who inject drugs reported a change in drug use behavior and 77% indicated increased perceived overdose safety by using fentanyl test strips.²³² At a harm reduction site in British Columbia, Canada, 36% of participants reported planning to reduce their drug dose while 11% planned to dispose of their drug after testing for fentanyl.²³³ These findings were mirrored in a study of PWID in Baltimore, Boston, and Providence, which found that over half of respondents would utilize fentanyl testing every day.²³⁴ In Dayton, Ohio, a survey of SSP clients found that one in five did not use their drug supply after it tested positive for fentanyl, and of those who used the drug differently, two in three reported that they used a lesser quantity.²³⁵
71. In conclusion, abatement programs in the U.S. should include resources to further support harm reduction, including services to provide access to clean syringes and injection equipment, safe disposal of used syringes, and screening and referral services to PWID that use heroin or fentanyl. Given the success of current SSPs, the substantial evidence base in promoting public health, and established cost-effectiveness in preventing the spread of disease and linking individuals to treatment, SSP services should be implemented across the U.S. SSPs should provide continuous services at consistent locations and hours using different approaches including permanent SSP sites and mobile SSP units, generally vans. Similarly, overdose prevention sites are a cost-effective option for communities to prevent overdose, reduce public drug consumption, and link difficult to reach individuals to services and treatment. Such programs should include increased availability of drug checking services to assist users in knowing when fentanyl may be present within drug supplies. It is also crucial that outreach, advertising, and education be incorporated into the SSPs in order to reach clients and provide awareness to local communities.

CONFIDENTIAL

E. PRESCRIPTION DRUG MONITORING PROGRAMS

Prescription drug monitoring programs (PDMPs) house data regarding the dispensing of controlled substances and make this information available to prescribers, pharmacies, and law enforcement.²³⁶ One purpose of PDMPs is to reduce opioid overprescribing. Healthcare providers can utilize these electronic databases to recognize patients who are a risk of overdose.²³⁷ The goal of this remedy is to ensure that prescribers across the U.S. and other relevant stakeholders are using available PDMP data to make informed clinical decisions.

72. PDMPs are an important tool for prescribers and health professionals to use to prevent opioid overdose. Although there is conflicting literature on the impact of PDMPs, evidence suggests that PDMP implementation is associated with decreases in opioid prescribing, morbidity and mortality,^{238,239,240,241} especially in the setting of states' legal requirements that health care providers query a PDMP in at least some circumstances.²⁴² One study found that PDMPs were associated with a reduction in opioid-related overdose deaths.²⁴³ Another study found that PDMPs were associated with reductions in the opioid prescriptions, opioid-related hospitalizations, and opioid-related emergency department (ED) visits.²⁴⁴ PDMPs in many states include data on prescriptions for Schedule II-IV controlled medications and update daily on a frequent (daily or weekly) basis.²⁴⁵ PDMPs differ across states in organization and operation.²⁴⁶ While they are a potentially valuable component of state's efforts to abate the opioid epidemic, it is crucial that they are used universally by providers before prescribing opioids in most circumstances, are updated with real-time data, and are actively used as a public health tool to identify patients at risk of overdose and inappropriate prescribing trends.²⁴⁷
73. Data integration is crucial to supporting the effective utilization of PDMPs. Health professional access to the PDMP must be streamlined and efficient, with data integration within electronic health record (EHR) and pharmacy systems. For example, use may significantly decline if the PDMP requires a separate login from the main EHR system;²⁴⁸ a randomized control trial found a 60% increase in the number of monthly PDMP queries among clinicians with an integrated PDMP and EHR relative to those who did not have an integrated system.²⁴⁹ These findings suggest that increasing direct access to PDMPs may help to improve adherence to guidelines and best prescribing practices.
74. In conclusion, abatement programs across the U.S. should include resources to further support prescriber utilization and benefit of PDMPs. It is important to note that the full benefit of PDMPs come when providers actively use the information and check the PDMP before prescribing opioids.^{250,251} Therefore, it is important that prescribers and health professionals continue to receive training on PDMPs to encourage its use. Additionally, PDMP data should be integrated into other data systems, such as EHRs and pharmacy systems.

CONFIDENTIAL

F. COMMUNITY PREVENTION AND RESILIENCY

The goal of community prevention and resiliency programs is to form coalitions to support the implementation of evidence-based, culturally-responsive interventions that reflect the values, capacities and expressed needs of local communities. These programs seek to strengthen social bonds and promote healthy behaviors. In doing so, these programs bolster the resiliency of a community by mitigating the clinical, social and economic impact of the opioid epidemic in local communities.

75. Prevention science. The field of prevention science has flourished in the past few decades and it offers important lessons for communities. This is because a growing body of scientific evidence demonstrates that problematic behaviors of individuals, such as among adolescents, can be mitigated through prevention efforts. Through these scientific investigations, researchers have also identified risk and protective factors, which has allowed for rigorously-designed experimental evaluations of administratively feasible, community-based interventions.^{252,253,254} While many such interventions have focused on violence or delinquency, others have addressed substance use disorders and demonstrate enduring benefit.^{255,256}
76. Community coalitions. Many approaches to primary prevention of substance use disorder (SUD) have been proposed. Some of the most promising are based on the use of community coalitions.^{257,258} The use of such coalitions provides one pragmatic and tested framework to identify community prevention needs, and to effectively implement durable, evidence-based interventions that command broad community support. Such efforts are designed to field durable, evidence-informed, and administratively feasible interventions that engage a diverse community coalition, and that effectively draw upon existing assets to meet the expressed needs of local communities.²⁵⁹ The broader community includes many entities that would be strong partners in such efforts, such as those from the business sector who may be key to implementing recovery-supportive workplaces (see Section 2E). Local nonprofits and government organizations contain the local knowledge necessary to coordinate this effort in collaboration with outside researchers, community residents, and other stakeholders.
77. One prominent collaborative approach that coalitions can use to develop and implement effective programs is the Communities that Care (CTC) model. The CTC model, which has been used to prevent or reduce substance use, delinquency and/or other risk behaviors,²⁶⁰ provides a structure for engaging stakeholders and establishing a shared vision for the community. CTC provides tools to survey community members regarding pressing local needs and provides one well-studied process to pursue specific and measurable goals in partnership with experienced intervention researchers. Rather than being proscriptive, the CTC model provides local communities with a menu of evidence-based approaches, from which the coalitions can identify specific interventions and strategies in the formulation, and iterative evaluation, of a community action plan to address local needs.
78. CTC's effectiveness was tested in the Communities Youth Development Survey (CYDS), a randomized control trial of 24 urban and rural communities in seven states (Washington, Illinois, Kansas, Colorado, Maine, Oregon, and Utah).²⁶¹ Outcomes by grade 12 were compared among youth who had received CTC interventions between fifth and ninth grade, and youth who resided in control communities. Youth within the CTC treatment group were significantly more likely to have refrained from any alcohol, tobacco, or other drug use, and were significantly less likely to have committed an act of delinquency.^{262,263,264,265,266,267,268} At an average inflation-adjusted cost of roughly \$633 per

CONFIDENTIAL

youth, CTC has demonstrated cost-effectiveness, returning an estimated \$5.30 for every dollar invested through reduced crime and criminal justice costs and other benefits to local communities.^{269,270}

79. Community resiliency coalitions should build on the areas of need, identifying key stakeholders, evaluating and implementing evidence-based programs using a systematic and iterative process such as the CTC framework. There are five major components to consider when moving forward with a community prevention and resiliency plan: (1) staffing; (2) assembling pertinent stakeholder coalitions; (3) surveying community members to identify needs and assets; (4) formulating and implementing a community action plan; and (5) evaluating processes and outcomes associated with the community action plan. Staff devoted solely to the implementation and coordination of community prevention efforts will ensure efficiency and prevent duplication.
80. In conclusion, abatement efforts in communities should encompass coalition building that focuses on promoting community resiliency. Programs that strengthen social bonds and promote health behaviors will help to heal the community-level trauma caused by the opioid epidemic. Frameworks such as CTC that incorporate measurable goals, are guided by local data and trends, and select evidence-based prevention programs have reduced substance use and reinforced social bonds within communities. A robust evidence base exists for the effectiveness and economic benefits of such efforts.

CONFIDENTIAL

G. LEADERSHIP, SURVEILLANCE, AND IMPLEMENTATION

The goal of surveillance is to convert local data to actionable intelligence at a local level by gathering, curating, and disseminating timely information about key dimensions of the epidemic to public health officials, policymakers, and other stakeholders. This is important because the absence of timely, granular information about the epidemiology of opioid use, addiction, and overdose at a local level has limited the ability of stakeholders to rapidly design, iterate, and evaluate targeted interventions to address the epidemic in the U.S. However, in addition to surveillance, resources are needed to support the continued development and evaluation of innovative programs responsive to the changing dynamics of the nation's opioid epidemic. Finally, leadership, including comprehensive planning and multi-agency coordination, is important to maximize efficient use of constrained resources to address the epidemic.

81. The opioid epidemic is a complex phenomenon with many different dimensions and impacts, and while it continues to change and evolve at a national and state level, at a local level these changes have often been even more profound. One consequence of this is that policymakers and public health officials need timely and accurate information on key parameters they can use to make informed decisions about resource allocation.²⁷¹ For example, the deployment, targeting, and evaluation of academic detailing programs depends vitally on timely information regarding opioid prescribing across prescribers. Similarly, naloxone distribution and training should be designed based on the relative incidence, causes, and outcomes of overdose within small, well-defined geographic areas.
82. These methods of assessing the opioid epidemic are important and should be expanded to include other important dimensions of the crisis, including measures that allow for near real-time, integrated assessment of prevention, treatment, and recovery. Such data can be drawn from medical, behavioral, and criminal justice systems, and include, but not be limited to, measures such as: opioid and non-opioid analgesic prescribing, OUD treatment capacity, MAT use and persistence, non-fatal and fatal opioid overdose events, naloxone distribution and use, criminal justice offense type, sentencing, treatment received while under court supervision (e.g., mandated treatment) and reoffending rates. Valuable information can be compiled from national, state, and local levels. For example, clinical information can be derived from PDMPs, emergency medical services, and hospital and emergency administration data. Behavioral health data can be drawn from sources such as the minimum data sets that are directly collected by all Single State Authorities (e.g., state agencies on drug abuse) for specialty treatment programs and from Medicaid programs, as well as from sources such as the Drug Enforcement Agency's National Technical Information Service (NTIS) database of waived prescribers and state and federal databases on specialty treatment providers (e.g., the SAMHSA treatment locator which is updated annually and provides street addresses for treatment programs). Criminal justice data from jails or prisons should also be integrated into local data ecosystems in order to ensure individuals who are incarcerated or newly released receive treatment and other important services.
83. There is no question that the collection, curation, and integration of these data will require substantial cooperation, effort, and tenacity. Many of these data systems are maintained by different private or public entities, and in some cases, significant administrative, legal, and cultural barriers will have to be overcome. However, there is tremendous promise in such efforts, especially since the effects of the opioid epidemic, and remedies to abate it, extend across medical, behavioral, and criminal justice systems. Linkage of these data will provide a more comprehensive understanding of the current issues associated with the epidemic and identify areas where local communities should focus.

CONFIDENTIAL

84. For example, consider the case of policing, where public health oriented policing interventions, such as a focus on overdose deaths, use of naloxone, education regarding addiction and stigma, and treatment on demand, can play an important role in reducing opioid-related injuries and overdose deaths.²⁷² Routine tracking of measures that evaluate these and other approaches can be used for a number of purposes including to establish benchmarks, allocate resources, and evaluate the success of new initiatives with respect to process, such as how many doses of naloxone have been dispensed, and outcomes, such as how many overdoses have been reversed. Medical examiner data is another important source of information to be incorporated into any surveillance system.
85. Data Ecosystems. Since the opioid epidemic impacts many different sectors, data sharing and integration, as part of a “Data Ecosystem”, can be used to support surveillance and program evaluation. For example, the Delaware Opioid Metric Intelligence Project integrates data on overdose deaths, toxicology reports, criminal incidents and arrests, population characteristics, and community resources into a user-friendly dashboard that displays several years of data.^{273,274} By contrast, the Florida Drug-Related Outcomes Surveillance and Tracking System is a data warehouse that integrates information from a variety of sources, including medical examiner and PDMP data, to enhance surveillance and collaboration amongst public health and criminal justice agencies.^{275,276} In Rhode Island, the Executive Office of Health and Human Services Data Ecosystem connects information from programs and external data sources into user-friendly data tools that can be used by state and non-state partners, such as program managers, researchers, providers, health insurers, and others.^{277,278} The Data Ecosystem has been used to understand Rhode Island’s overdose and addiction crisis; for instance, an analysis of data from Medicaid, the Department of Labor and Training, the Department of Corrections, the Department of Human Services, and the All-Payer Claims Database yielded findings about the risk and protective factors for non-enrollment in MAT.^{279,280} Another way data integration is important is for early detection of novel analogs and rapid communication of this information.²⁸¹ Together, these measures can support a more effective, efficient, and data-driven response to the opioid crisis.
86. Governance. Surveillance must be combined with leadership and a cohesive, multidisciplinary team should coordinate a given community’s response across multiple agencies, departments, and stakeholders and be based on a comprehensive needs assessment. Representation, and appropriate staffing, from key entities such as the medical, behavioral, and criminal justice systems within the community is vital. The overall effectiveness of a community’s response will rest in part upon the relationships among those coordinating the effort, and the overall coherence and shared vision among relevant parties. This team should meet regularly to review programs and policies, as well as assess surveillance data and emerging evidence from the field. In addition to serving as liaisons to their respective organizations, as well as more broadly championing the community’s strategic response, the team should troubleshoot, redirecting resources and re-engineering how individuals with chronic pain, non-medical opioid use or OUD are identified and managed within relevant systems of care.
87. Abatement efforts across the U.S. should build upon the current surveillance and data sources by allocating sufficient resources to support a dedicated team of professionals to review and synthesize data, and to make recommendations for abatement efforts. This team may include individuals such as epidemiologists, data scientists, and community liaisons, such as law enforcement experts and community advocates, and should focus on: (1) improving the timeliness, quality, coordination and

CONFIDENTIAL

integration of existing data streams (e.g., surveys, mortality records, etc.); (2) conducting opioid-specific surveillance activities to better understand key aspects of the dynamic nature of the epidemic that are not visible through existing data channels; (3) enhancing the accessibility, visibility, and shareability of data related to the epidemic through multi-agency coordination, preparation of reports and data summaries, creation of dashboards, and responses to data requests from relevant stakeholders; and (4) performing comprehensive evaluations of interventions and proposing evidence-based recommendations so as to maximize further returns. Quality surveillance data and dissemination is key to identifying and responding to changing needs within local communities. In response to the continually evolving opioid epidemic, abatement efforts should support the development and evaluation of innovative programs that seek to prevent, mitigate, and address harms caused by opioids.

88. In conclusion, abatement programs should include resources to support the further development and management of state-of-the-art surveillance programs that can serve as mission control centers as remedies are deployed, iteratively refined and evaluated. Such resources should allow for relevant data from a variety of local, state, and national sources to be gathered, curated, integrated, and analyzed, and in turn, reported back out using a variety of different approaches customized to the specific needs of key stakeholders such as public health officers, treatment providers, and law enforcement officials. Remedies should also include resources to support the leadership that will be needed for a well-coordinated, longitudinal, multi-stakeholder initiative. Additionally, the development of novel approaches to engage and support individuals with OUD should be leveraged in order to respond to the changing dynamics of the local opioid epidemic.

CONFIDENTIAL

CATEGORY 2: TREATMENT – SUPPORTING INDIVIDUALS AFFECTED BY THE EPIDEMIC

This category of my Abatement Plan seeks to better identify individuals with OUD and to remove clinical, economic, and social barriers diminishing their access to comprehensive, coordinated high-quality care.ⁿ One important principle is to close treatment gaps. However, many other interventions are necessary in addition to the closure of treatment gaps, including a transformation of the delivery system of care so that it “mainstreams” addiction care and delivers it as consistently and compassionately as it does care for pediatric cancer or amyotrophic lateral sclerosis (ALS).

A. CONNECTING INDIVIDUALS TO CARE

The goal of this remedy is to address the widespread treatment gaps that prevent so many from seeking or being retained in care. For example, studies show that some individuals who overdose in the field are not formally evaluated or successfully linked with treatment,^{282,283} while many others, even if brought to an Emergency Department, are discharged rather than receiving a warm handoff to an inpatient or outpatient treatment facility.²⁸⁴ There are opportunities to improve the identification and treatment of individuals with OUD in many different settings, and thus multiple methods are needed to connect people to services, ranging from helplines and “bridge programs” to Overdose Response Teams that proactively reach out to individuals after an overdose or other acute opioid-related harm.^o

89. Helplines. Helplines have been used as an effective tool for delivering information to people in crisis for decades, assisting callers by linking individuals to care and resources to address their individual circumstance. Helplines serve as an inexpensive, efficient, and immediate source of information for individuals affected by SUD. Ideally, helplines should be a 24-hour phone, text, and chat line designed to streamline the process of accessing treatment for substance use disorder and behavioral health. Staff should be comprised of social workers that provide direct transfers to withdrawal management facilities and referrals to inpatient treatment, sober living homes, medications for addiction treatment, outpatient therapy and support groups. After linking callers to resources, staff should follow up with callers at designated intervals to ensure their needs are being met.
90. Helplines serve as a vital link for individuals with OUD and their loved ones. For example, in 2019, more than 11,000 individuals called a helpline established within the State of West Virginia, of which 75% called on behalf of themselves and 13% called on behalf of a family member.²⁸⁵ Opioids were the most commonly used substance among helpline callers (40%). Over 14,000 callers have received a “warm hand-off” to a service provider through this helpline,²⁸⁶ nearly 2% have been referred for MAT, and 43% for management within a detoxification center; of those seeking detoxification, many were able to enter a treatment program within 24-hours.²⁸⁷ This helpline serves as an excellent example to scale nationally as staff are also available to assist callers with Medicaid or private health insurance enrollment. A helpline is one tool to address barriers for those with OUD in finding timely linkage and entry into treatment. Importantly, a helpline may serve as another source of data for policymakers to identify trends in drug use, treatment needs, and capacity building.

ⁿ It is also important to consider individuals with opioid dependence and non-medical use who may not yet fulfill formal criteria for an OUD; I address these individuals in Section 2C.

^o Ensuring adequate staffing of social workers, case managers, and addiction counselors in clinical, behavioral, criminal justice, and community settings is also vital and discussed elsewhere in my report

CONFIDENTIAL

91. Peer support specialists, which include peer recovery coaches and peer navigators, provide another promising and cost-effective model to engage and serve individuals with OUD.^{288, 289} Paraprofessionals with lived experience in recovery can assist patients in accessing medication treatment, can help navigate barriers to treatment engagement and retention, such as provider stigma and transportation. These individuals draw upon their lived-experience and methods such as motivational interviewing to strengthen individuals' motivation to seek treatment and to remain engaged. Peer support specialists may provide a number of different types of resources or support to individuals with OUD, ranging from psychological support to connections to recovery communities, activities, and events.²⁹⁰ Two systematic reviews examining the impact of peer-recovery services suggest the positive impact that such services can have on those with substance use disorders.^{291,292}
92. Bridge programs. Emergency Departments represent a key setting to link individuals to treatment after an overdose.²⁹³ One randomized control trial found that patients who received ED-initiated MAT were two-times more likely to be engaged in treatment one-month after intervention, compared to patients that received a Brief Negotiation Interview or referral alone (78% vs 37-45%, respectively).²⁹⁴ While patients in all three intervention groups reported lower HIV risk behaviors, those that received ED-initiated MAT had lower self-reported opioid use one-month after baseline. A separate study found that patients who received ED-initiated MAT were 2.3-times more likely to engage in follow up treatment.²⁹⁵ Yet another study of three separate EDs found that among individuals who initiated buprenorphine in the ED, three in four attended OUD treatment the following day and three in five remained in treatment after one month.²⁹⁶ While there are different models of ED-based OUD treatment programs, important factors include: adequate OUD treatment capacity within the community; peer support services and a low-barrier approach; and efforts to address stigma and improve education of treatment options and efficacy.²⁹⁷
93. Hospital consultation services. Hospitalizations represent an opportunity to identify and triage patients with OUD into substance use treatment, but our healthcare system fragments care between general medical services and mental health services, which can pose a significant barrier to access. These types of programs are targeted towards hospitalized patients which aims to improve access to substance use services by connecting traditionally siloed medical care, addiction treatment, and community support.²⁹⁸ They are composed of a collaborative team that include addiction medicine physicians, nurse practitioners, patient navigators, and licensed vocational nurses, who are able to provide comprehensive substance use disorder assessment, initiate addiction treatment, and connect patients with community partners for additional substance use disorder services. In their first year, one such team serviced over 400 patients, doubled follow-up rates to community care, and helped 20 patients enter residential treatment.²⁹⁹
94. Drug sobering centers. It is crucial that individuals in crisis have access to places where they can recover, and when stabilized, be connected to services for further support. The drug sobering center is a non-medical, social model program staffed by health workers focused on harm reduction, safety, and low-threshold engagement.^p One example of this type of setting are sobering centers, which serve as an alternative to jails and EDs by providing a safe place for individuals to recover from intoxication

^p There are other types of settings that connect individuals in crisis to immediate care, as well as linkages to long-term services. For example, in Rhode Island, BH Link runs a 24/7 community-based walk-in triage center, where clinicians can link individuals to long term care and recovery supports. (BH Link. What is BH Link?. Available at: <https://www.bhlink.org/about-1>. Accessed May 26, 2021.)

CONFIDENTIAL

while under observation.³⁰⁰ This is important, as individuals who are intoxicated or under the influence of substances are vulnerable to many potential harms. Historically, sobering centers have primarily served alcohol-dependent individuals and have been shown to be cost-effective due to the reduced strain on health care and law enforcement resources.³⁰¹ Similar to overdose prevention sites, sobering centers serve as an opportunity to connect marginalized populations to other health care services. For example, one California sobering center was established in 2003 with the goal of providing health care to alcohol-dependent clients and decreasing alcohol-only-related ED admissions and ambulance transports.³⁰² Between 2013 to 2016 the center received 11,596 visits, with most clients (~95%) completing care at the sobering center without requiring ED evaluation.³⁰³ It is notable that those sobering from drugs such as opioids may have different needs than those sobering from alcohol, suggesting the value of centers with experience managing those with opioid-related intoxication.³⁰⁴

95. Overdose Response Teams (ORTs). Sometimes known as a Quick Response Team (QRT), Drug Abuse Response Team (DART), or Street Opioid Response Team (SORT), these teams generally consist of a first responder, addiction counselor, and peer support specialists and are similar to rapid-response, mental health evaluation teams. Increasingly, community paramedics have been included in ORTs to provide appropriate clinical intervention and care coordination for individuals who have recently overdosed.^{305,306,307} These teams are designed both for first response to narcotic-related emergencies, as well as to approach overdose victims during “recovery windows”, a 48- to 72-hour period following an overdose when individuals may be most amenable to entering treatment.³⁰⁸ In such cases, based on referrals from EMS or family and friends, the ORT seeks to make contact with the individual, and if they accept treatment, the ORT arranges for them to quickly enter treatment. If the ORT is unable to make contact, they leave treatment information behind. Because of their timely response as well as multidisciplinary composition, these teams are one means of helping to strengthen the community-individual relationship as well as to bridge one treatment gap that prevents many individuals with OUD from seeking care.
96. Mobile treatment units. Mobile treatment units, also known as mobile health units, mobile medication units, or mobile medical teams, seek to expand treatment access by delivering services to hard-to-reach populations and underserved communities.³⁰⁹ Mobile treatment units can be used to increase access to OUD treatment in both rural and urban settings,^{310,311} and there is growing experience with them around the country, including programs in Philadelphia,³¹² Connecticut,^{313,314} Maryland,³¹⁵ and Colorado.³¹⁶ In Maryland, the Eastern Shore Mobile Care Collaborative at Caroline County Health Department provides a mobile treatment unit that links individuals with OUD in underserved rural areas with MAT.³¹⁷ A nurse and peer recovery specialist staff the unit, and use a secure, HIPAA compliant videoconferencing technology to connect patients to an addictions medicine specialist at the University of Maryland, School of Medicine in Baltimore. Between February 1, 2019 and June 30, 2020, 118 patients with an OUD were enrolled, of which 94 patients primarily received treatment through the MTU.³¹⁸ Of these 94 patients, more than half (55 patients; 58.5%) were retained in treatment and opioid use decreased by 32.8% in the 90 days following enrollment. The Colorado Department of Human Services, Office of Behavioral Health used a State Opioid Response grant to provide six mobile health units staffed by a nurse, licensed addiction counselor, and peer recovery coach;³¹⁹ services are also available via pop-up clinics set up at local organizations.^{320,321} The program provided MAT services to 48 rural towns between October 2019 and September 2020.³²² During this period, the program provided services to 414 unique clients through 2,015 clinic visits. It

CONFIDENTIAL

has been estimated that approximately 14% percent of individuals live in rural communities across the U.S.³²³ Rurality poses several challenges to individuals seeking treatment for OUD, including lack of providers and clinics, as well as longer travel times.³²⁴

97. Transportation. Transportation can represent a significant barrier for those with OUD to access and adhere to treatment.³²⁵ Though public transportation may be available within cities, those that live outside urban centers may not have consistent or reliable transportation needed to attend treatment, thereby reducing the likelihood that they will be able to adhere to treatment. Also, factors such as inconsistent scheduling or proximity to the appropriate bus or train line can be an added barrier to those in treatment, even within urban areas. Transportation needs remain for other individuals as well, such as those accessing harm reduction services or for pre- and post-natal appointments for women with OUD. Providing travel vouchers, reimbursing taxi or ride-sharing costs, or providing gas cards are additional options to improve access to such services.³²⁶
98. In conclusion, abatement programs must support both the linkage of individuals to care and their retention once in treatment and recovery. Helplines, peer recovery coaches, ORTs, mobile treatment units, drug sobering centers, bridge programs, hospital consultation services, drop-in centers, community paramedicine programs, proactive street outreach, and transportation initiatives are examples of effective and established tools to link individuals to treatment. Since people who use drugs may be difficult to reach, efforts that build rapport and maximize the quality of interactions are crucial. There are also key reachable moments, such as during hospitalization and “recovery windows” following an overdose, when people who use drugs may be most amenable to initiating treatment. Retention in treatment must be supported by transportation assistance and other measures to increase access, ensuring smooth transitions across the continuum of care and through peer-support.

CONFIDENTIAL

B. TREATMENT FOR OPIOID USE DISORDER

Though there have been efforts to scale up treatment for those with OUD, more investments are needed so as to fulfill the overarching goal of this remedy: the provision of readily accessible treatment to patients with OUD. Such treatment should include low-barrier access to FDA-approved MAT for use in individuals with OUD, since these are efficacious treatments that not only reduce the likelihood of opioid use, but also the risk of overdose, criminal activity, and the transmission of infectious disease.³²⁷ However, not everyone with OUD requires MAT, and even when it is provided, it should be part of a full continuum of care, including care that addresses other acute, chronic, and preventive needs. Despite efforts to increase access to MAT, medication for OUD remains underutilized among adolescents and adults in the U.S. who may benefit from treatment.³²⁸

99. The FDA has approved three medications for the treatment of OUD and the choice of medication should be tailored to the unique needs of each individual.³²⁹

- 1) Methadone is an opioid agonist, which means it can activate opioid receptors in the brain and provide pain relief similar to other opioids. It can prevent withdrawal symptoms, reduce cravings and block the euphoric effects of other opioids. Its dispensing for OUD is limited to certified opioid treatment programs (OTPs), serving as a barrier to broader use.^{330,331}
- 2) Naltrexone is an opioid antagonist that blocks the effects of other narcotics. Provided as a daily pill or monthly intramuscular injection, it can be prescribed in ambulatory settings and does not have any abuse or diversion potential.³³² However, it cannot be administered to individuals with opioids in their systems, since doing so will precipitate abrupt opioid withdrawal.³³³
- 3) Buprenorphine is a partial agonist and partial antagonist of the opioid receptor, with significantly lower potential to produce euphoria or respiratory depression than other opioids. Appropriately waived physicians may prescribe buprenorphine in offices, community hospitals, or correctional facilities.³³⁴ While the main form of buprenorphine for OUD is an orally administered combination of buprenorphine and naloxone (the latter of which is an opioid reversal agent as described in Section 2F), other formulations of buprenorphine are FDA approved, including an extended-release injection and implant.³³⁵

100. Historically, some have opposed MAT based on a number of misconceptions, including that it is invariably diverted (it is not, and when diversion does occur, it is often to avoid the dysphoria of opioid withdrawal including symptoms such as agitation, anxiety, muscle aches, nausea, and vomiting),⁹ or that it is simply substituting one addiction for another (it is not).³³⁶ Rather, MAT increases social functioning and retention in treatment, allowing individuals a better opportunity to reintegrate within their families and communities and to transition from active addiction through treatment into recovery.^{337,338} It is also associated with a wealth of other positive outcomes, including decreased opioid use and improved survival.³³⁹ Because of this, its use is supported by numerous authoritative sources, including the CDC, National Institutes of Drug Abuse, American Society of Addiction Medicine, and SAMHSA. It is also supported by global authorities such as the World Health Organization, which includes buprenorphine and methadone as Essential Medicines.³⁴⁰ However, as I discuss further in Paragraph #105, MAT is not a stand-alone therapy nor does everyone

⁹ Even the need for such defense of MAT underscores the marked stigma and asymmetry that exists between OUD and other diseases; for example, it is hard to imagine a setting where the use of inhalers for asthma, insulin for diabetes, or even psychotropics for mental illness, would be met with such skepticism or outright opposition.

CONFIDENTIAL

require it; when it is used, it must be accompanied by other clinical interventions as part of comprehensive care for those with OUD.

101. Despite the potential of MAT to help address the opioid epidemic, it is severely underutilized. For example, an analysis of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) indicated that fewer than one in five individuals with non-medical prescription OUD were ever treated,³⁴¹ and rates of use of MAT within publicly funded treatment programs have historically been low.^{342,343} Combined with low use of MAT even within programs offering it, some estimates are that as few as one in ten individuals with OUD receive MAT.³⁴⁴ Worsening matters further, treatment courses are often short, with rates of treatment discontinuation and relapse high,³⁴⁵ and even periods of MAT use are often punctuated by the receipt of prescriptions for non-MAT opioids, underscoring common and serious lapses in care even for those accessing these treatments.^{346,347}
102. A 2018 study from Massachusetts provides useful context for the benefits of MAT in decreasing mortality.³⁴⁸ In this analysis of adults who survived an overdose between 2012 and 2014, in the 12 months after an overdose, 11% received methadone, 17% received buprenorphine, and 6% received naltrexone. The median duration of treatment was short, between one to five months. Both methadone and buprenorphine utilization were associated with decreased opioid-related and all-cause mortality.^r Thus, this study underscores: (a) large gaps in MAT adoption; (b) high discontinuation rates; and (c) the life-saving benefit of methadone and buprenorphine. One systematic review and meta-analysis found that the risk of all-cause mortality was six-times higher within the four-weeks following MAT cessation and remained double the rate for the remainder of time that patients who are not treated with MAT.³⁴⁹
103. There are many barriers that account for the large gap between the number of individuals with OUD and the proportion that are treated with MAT. Underlying these barriers are misconceptions about the nature of OUD and the effectiveness of MAT, as well as other concerns such as those identified in Paragraph #129. In a 2019 study based on national surveys, my colleagues at the Johns Hopkins Bloomberg School of Public Health found that only about one in three substance use treatment facilities offered MAT in 2016, and fewer than one in sixteen (6.1%) offered all three treatment medications.³⁵⁰ There is also a large shortage in the number of providers who are equipped to provide care for those with addiction.^{351,352} Finally, the costs of MAT, as well as other treatments for OUD, have historically been an impediment for many individuals who might otherwise seek care.³⁵³ While our own work,^{354,355} and that of others,³⁵⁶ suggests that health plans are increasingly modifying their coverage and reimbursement policies so as to address the opioid epidemic, many individuals with OUD still face economic barriers to treatment, with a 2016 Department of Defense estimate of the costs of MAT³⁵⁷ exceeding that of diabetes mellitus (\$3,560) or kidney disease (\$5,624).³⁵⁸
104. Overcoming these economic and structural barriers is just the first step in achieving the potential for high quality OUD care.³⁵⁹ This is because there is enormous stigma associated with opioid addiction, which discourages patients from seeking treatment and discourages clinicians from providing it (also see Paragraph #26).³⁶⁰ While OUD is a brain disease, it is often framed as a moral failing instead; treatment systems remain marginalized rather than “mainstreamed”; language about “legitimate pain”

^r The authors speculated several reasons they may not have observed a statistically significant benefit with naltrexone, including a small sample and short duration of use, with most patients receiving it for a single month. In addition, the study was unable to differentiate oral from intramuscular naltrexone.

CONFIDENTIAL

and “junkies” and “getting clean” perpetuates such marginalization; and many features of the criminal justice system’s intersection with OUD also contribute to the persistent organizational failures that are seen.³⁶¹

105. Investments in the treatment infrastructure must be made along a full continuum of care, from overdose reversal to support that enables long-term recovery. Individuals with OUD need regular contact with health care professionals responsible for supervising their pharmacologic and/or behavioral treatments, screening for adverse events or treatment failures, and delivering supportive care and psychological counselling. In many ways, such a model is no different than a model of care for someone with asthma or diabetes. These diseases, and their treatments, cannot be managed in a vacuum. Medications, whether MAT or treatments for other chronic diseases, should be provided in the context of a therapeutic relationship where risk factor attenuation, supportive counseling, medication monitoring, and attention to other health care needs take place. In the case of OUD, the delivery of structured social support and counseling may be especially important, given that these engagements assist patients in establishing the social reconnection that can be critical to long-term recovery. Treatment must also recognize the importance of screening and treatment for infectious diseases such as hepatitis C and HIV,³⁶² as well as attending to chronic pain, other substance use disorders, and mental illness, all of which are common among individuals with non-medical opioid use or OUD.³⁶³
106. In addition, no single treatment is right for everyone, and not every individual with a history of OUD should be treated with MAT. For example, some people have a remote history of OUD and while they retain a lifelong sensitivity and vulnerability to opioids, just as an alcoholic does to alcohol, many of these individuals are living productive, successful lives in recovery without MAT. Some individuals have been treated with MAT but successfully tapered off of such treatment while maintaining a healthy recovery through abstinence-based, 12-step programs such as Narcotics Anonymous, psychological counselling, and supportive therapy, or combinations of these or other approaches.
107. There are many different models for expanding access to OUD treatment, and this remains an area of rapid growth and program evaluation nationwide. For example, Office-Based Opioid Treatment (OBOT) allows for physicians completing a waiver program to prescribe buprenorphine for OUD within primary care settings; the Medicaid Health Home Model integrates MAT and behavioral health treatments with primary care for people with OUD; and the Hub-and-Spoke Model triages patients between primary care clinics for the treatment of uncomplicated OUD (the “spokes”) and centralized clinics equipped to care for patients requiring methadone or whose complex behavioral and medical needs exceed those routinely provided in primary care settings (the “hub”).³⁶⁴ Other models are based on ED Bridge Programs as described in Section 2A.³⁶⁵
108. Models that rely more heavily on telemedicine for MAT supervision are also increasingly common, especially as a result of the COVID-19 pandemic.^s In response to the COVID-19 pandemic, the DEA modified several policies that help facilitate the delivery of MAT via telemedicine. These include:

^s For example, my colleagues and I estimated a 7,360% increase in the prevalence of telemedicine visits for OUD from April to June of 2020, compared to the same timeframe in 2019 (Mansour O, Tajanlangit M, Heyward J, Mojtabei R, Alexander GC. Telemedicine and Office-Based Care for Behavioral and Psychiatric Conditions During the COVID-19 Pandemic in the United States. *Annals of Internal Medicine*. 2020:M20-6243.)

CONFIDENTIAL

allowing for prescribers to prescribe buprenorphine to new patients, and to renew such prescriptions, using telemedicine without requiring an in-person medical evaluation;^{366,367} health practitioners who do not have a buprenorphine waiver may administer buprenorphine to patients with OUD under special circumstances;³⁶⁸ and stable patients may receive 28 days of take-home MAT.³⁶⁹ Beyond the pandemic, telemedicine may increase the accessibility of MAT and treatment retention by overcoming transportation barriers as well as making MAT more available in settings where there are shortages of health care providers. Of course, despite the potential benefits of telemedicine, there are several reasons that it may not be a suitable means of clinical care for particular individuals, such as those uncomfortable with the technology or with complex comorbid illness where face-to-face evaluation may be especially important.

109. Treatment programs differ along many dimensions, such as the degree to which they focus on the delivery of pharmacotherapy, behavioral services, care integration, and community-based education or outreach. It is important that some programs are designed to deliver care to individuals who have initiated MAT, or “induction”, in low-barrier settings such as syringe services programs or EDs, given that the marginalization and social isolation of some of these individuals increase their likelihood for relapse or treatment discontinuation.
110. Most individuals with OUD who are entering treatment can be managed either in an ambulatory or intensive outpatient (IOP) setting, although initial evaluation and appropriate triage is important so as to optimize each individual’s likelihood of successful treatment and recovery. IOP programs typically provide for several hours of patient engagement four to five days per week for a period of several weeks, and may include services ranging from individual, group and/or family counseling to case management to vocational training and employment services.³⁷⁰ A minority of individuals with OUD require inpatient hospitalization for initiation of treatment, such as when acute illness (e.g., pneumonia or soft tissue infection), advanced comorbid disease (e.g., heart failure or liver failure), or uncontrolled psychiatric illness (e.g., bipolar affective disorder) makes ambulatory or IOP treatment unfeasible.
111. Assertive Community Treatment. Some individuals with OUD require more intensive care due to their co-occurring mental health conditions and other factors, such as recurring incarceration and/or homelessness, which complicate their treatment. For example, psychiatric comorbidities, which are prevalent in almost 65% of individuals with OUD, have been associated with increased likelihood of treatment discontinuation.^{371,372,373} For these individuals, the Assertive Community Treatment (ACT) model has been shown to be effective in improving their treatment outcomes^{374,375} and ultimately cost-effective to the community overall.^{376,377} Through this model, an interdisciplinary team with a psychiatrist, two psychiatric nurses, two employment specialists, two SUD specialists, a peer recovery coach, an administrative program staff, and social workers or other masters or doctoral level professionals, work with clients to provide comprehensive and intensive services.³⁷⁸ These services include assistance with activities of daily living, substance use and mental health treatment, employment support services and developing other recovery skills, administration and monitoring prescriptions, and provision of interventions with support networks as needed.
112. In conclusion, abatement programs should include further investments in the treatment system so as to allow for the provision of additional comprehensive, coordinated high-quality care for individuals with OUD, including access to services for the identification and management of acute, chronic, and

CONFIDENTIAL

preventive care needs.³⁷⁹ Such investments should also be targeted at each specific point where gaps occur or individuals otherwise experience unacceptably high rates of relapse or loss to follow-up, ranging from the identification and triage of patients after non-fatal overdose to the expansion of induction and IOP programs to the provision of compassionate, evidence-based care for individuals living in recovery. Efforts in the U.S. should also continue to scale telehealth services for individuals who would benefit from such technologies.³⁸⁰

CONFIDENTIAL

C. ADDRESSING NON-MEDICAL OPIOID USE

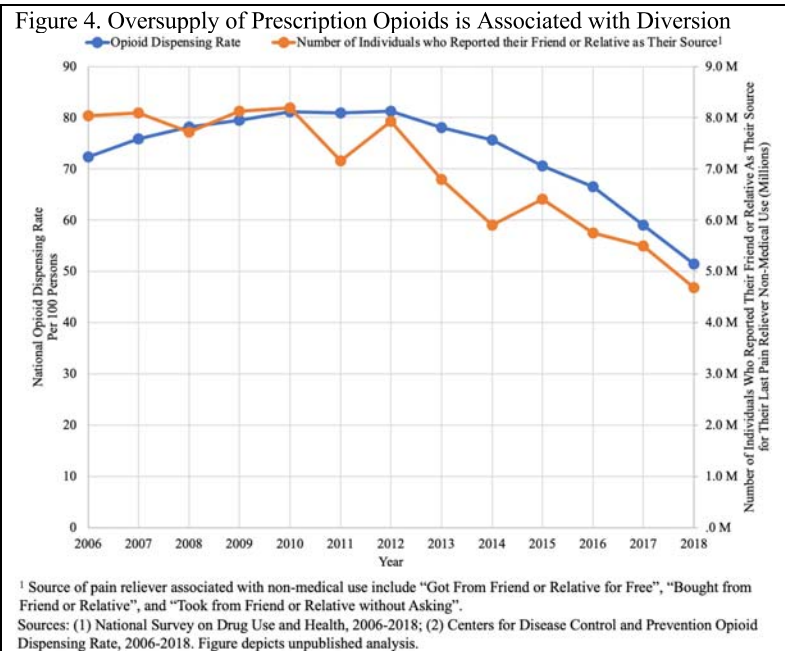
This abatement remedy focuses on individuals with non-medical opioid use. This category is important because many individuals engage in such non-medical use, and they are at elevated risk for a number of harms from opioids, including the development of OUD and overdose death.

113. Non-medical opioid use is defined by the National Institute on Drug Abuse as “taking a medication in a manner or dose other than prescribed; taking someone else’s prescription, even if for a legitimate medical complaint such as pain; or taking a medication to feel euphoria (i.e., to get high)”.³⁸¹ In contrast to OUD, which has formal diagnostic criteria according to the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5), non-medical opioid use is much more common and encompasses a broader continuum of behaviors. It is important to identify individuals with non-medical opioid use because they are at increased risk of opioid-related adverse events.
114. An estimated 9.5 million Americans, or 3.4% of the total population, reported non-medical use of prescription opioids or heroin during the past year based on 2020 data derived from the National Survey of Drug Use and Health (NSDUH).^{382,t} While this represents a modest decline from 2019, during which 10.1 million people were estimated to have engaged in past year non-medical opioid use, the numbers nevertheless remain staggering.³⁸³ Of these 9.5 million individuals, 97.5% engaged in past year non-medical use of prescription opioids, while 9.5% engaged in non-medical use of heroin and 7.0% engaged in non-medical use of both prescription opioids and heroin.³⁸⁴ Among adults with non-medical use of opioids in 2015 who did not have OUD, approximately two-thirds of cases reported the reason for such non-medical use was the relief of pain, highlighting the overlap of chronic pain with non-medical opioid use as well as the opportunities to address both simultaneously through well-designed abatement remedies.³⁸⁵
115. Several additional points regarding non-medical prescription opioid use are also important to consider. First, non-medical opioid use has historically tracked closely with prescription opioid oversupply. For example, **Figure 4** (next page) depicts the association between the national opioid dispensing rate³⁸⁶ and weighted estimates³⁸⁷ of the number of individuals reporting friends/relatives as their prescription opioid source from 2006 to 2018. Note that both prescription opioid supply and non-medical use peaked in approximately 2010-2011 and have declined in parallel fashion through 2018. Other data, such as the “Monitoring the Future Study”, a national survey of adolescents that is funded by the National Institute on Drug Abuse and conducted by the University of Michigan, support this observation, finding that non-medical prescription opioid use has steadily declined since 2010 as opioid prescribing volume has declined.³⁸⁸

^t It has been established and is accepted among the public health community that NSDUH significantly underestimates the true prevalence of opioid use disorder and heroin use disorder in the U.S. (Barocas JA, White LF, Wang J, Walley AY, LaRoche MR, Bernson D, Land T, Morgan JR, Samet JH, Linas BP. Estimated Prevalence of Opioid Use Disorder in Massachusetts, 2011-2015: A Capture-Recapture Analysis. *American Journal of Public Health*. 2018;108:1675-1681. Midgette G, Davenport S, Caulkins JP, Kilmer B. RAND Corporation. What America's Users Spend on Illegal Drugs, 2006-2016. https://www.rand.org/pubs/research_reports/RR3140.html.)

CONFIDENTIAL

116. In light of this, it should come as no surprise that the NSDUH consistently identifies prescribers as a common source of prescription opioids for non-medical use.^{389,390,391} Specifically, based on 2019 data, over one in three (37.5%) individuals reporting prescription opioid non-medical use in the past year obtained their prescription opioid from a prescriber,³⁹² an indication that the health care system, including high-prescribing clinicians, continues to play a role in fostering the epidemic.^u While half (50.8%) of individuals aged 12 years and older who report non-medical use of prescription opioids within the past year report that they obtained their prescription opioid from a friend or relative,^{v,w,393} nearly 90% of these friends and relatives reportedly obtained that opioid from a physician.³⁹⁴ The large oversupply of opioids in these settings supports the use of interventions such as prescription “caps” that states and some payers have implemented to reduce the volume of opioids prescribed for short-term use,³⁹⁵ as do several studies indicating that the likelihood of an individual converting to chronic opioid use is significantly greater among individuals receiving greater doses or durations of opioids on their first fills.^{396,397,398}



117. Another feature of non-medical use that is important to consider is that, according to data from the 2008 to 2011 NSDUH, as the intensity of non-medical opioid use increases, the likelihood of friends/family as a prescription source decreases and the likelihood of prescribers as a source increases (**Table 1**, next page).³⁹⁹ For example, note that as the number of days of non-medical use during the past year increases from 1-29 to 200-365, the proportion of non-medical users reporting they were given opioids by friends or family for free declines from 61.9% (95% confidence intervals [CI] 59.7-64.0%) to 26.4% (CI 20.9-32.9%), suggesting that there are different phenotypes of non-medical users, and that “gifting” of opioids from friends or family becomes less common as the intensity, and seriousness, of an individual’s non-medical use increases.

^u By contrast, 1.5% of those with opioid misuse report their source as from more than one doctor, again attesting to the relatively small contribution opioid shoppers make to the epidemic. (Chang HY, Murimi IB, Jones CM, Alexander GC. Relationship Between High-Risk Patients Receiving Prescription Opioids and High-Volume Opioid Prescribers. *Addiction*. 2018;113:677-686.)

^v 50.8% of individuals reported that the source of pain relievers for their most recent misuse was from a friend or relative. Overall, 37.0% obtained at no cost, 9.2% purchased from a friend or relative, and 4.6% took the pain relievers without asking.

^w Note that the oft-cited NSDUH data regarding source of non-medical use is often misinterpreted; the NSDUH does not capture the incident, or first, source of prescription opioids, nor the source of most frequent use, but rather, refers to the most recent source of prescription opioids within the previous 30-days (prior to 2015) or most recent source overall (2015 to present).

CONFIDENTIAL

Table 1. Source of Opioid Pain Reliever Most Recently Used by Frequency of Past-Year Non-Medical Use (from Table 2 in Jones et al, 2014)

Source	Nonmedical Use, % (95% CI)				
	Any (n = 11 018 735)	No. of Days Used			
		1-29 (n = 7 037 205)	30-99 (n = 2 110 122)	100-199 (n = 1 103 312)	200-365 (n = 768 096)
Given by a friend or relative for free	54.4 (52.9-56.0)	61.9 (59.7-64.0) ^b	48.5 (45.6-51.5) ^b	37.7 (33.0-42.5) ^b	26.4 (20.9-32.9)
Prescribed by ≥1 physicians	19.7 (18.4-21.1)	17.9 (16.2-19.7) ^b	19.5 (17.0-22.3) ^b	26.5 (22.2-31.4)	27.3 (22.3-32.9)
Stolen from a friend or relative	4.9 (4.4-5.3)	5.3 (4.7-6.0) ^b	4.6 (3.6-5.7) ^b	4.1 (2.7-6.0)	2.9 (2.1-4.1)
Bought from a friend or relative	11.3 (10.4-12.1)	7.6 (6.7-8.5) ^b	15.6 (13.4-18.0) ^b	18.3 (15.4-21.5)	23.2 (18.0-29.3)
Bought from a drug dealer or other stranger	4.2 (3.8-4.8)	2.1 (1.7-2.6) ^b	5.3 (4.1-6.9) ^b	8.2 (6.5-10.3) ^b	15.2 (12.0-19.1)
Other ^c	5.5 (4.7-6.3)	5.3 (4.3-6.4)	6.4 (5.4-7.7)	5.2 (3.5-7.8)	5.0 (2.9-8.4)

^a Obtained from the US National Survey on Drug Use and Health, 2008 through 2011.⁵^b Estimate is statistically significantly different from that for highest-frequency users (200-365 days) ($P < .05$).^c Includes written fake prescriptions and those opioids stolen from a physician's office, clinic, hospital, or pharmacy; purchased on the Internet; and obtained some other way.

118. Post-surgical oversupply of prescription opioids has also been strongly associated with diversion.⁴⁰⁰ There is a long history of opioid oversupply after surgery.^{401,402,403,404} Higher post-surgical opioid dose and duration has been associated with increased risk of chronic use.⁴⁰⁵ Additionally, most patients receiving opioids after surgery have leftover opioids⁴⁰⁶ that remain in their home⁴⁰⁷ and are often not safely stored or properly disposed.^{408,409}
119. In contrast to patients who are using opioids fully as directed under the care of a licensed prescriber, which still poses unacceptably high risks in many patients currently receiving them, patients with non-medical opioid use should be identified and targeted for early intervention so as to avert their potential transition to OUD or overdose. Methods to identify and address these patients include both the routine clinical use of PDMPs and clinical interviewing. Clinical interviewing is useful not only to screen for potential non-medical use but also to explore motivations for such and to address underlying issues, including sub-optimally treated pain, depression or other behavioral health factors that may be driving such behavior. Once identified, such patients should receive more intensive clinical monitoring, psychosocial interventions, pain management, and in some cases, transition to partial opioid agonists such as buprenorphine or tramadol.
120. In conclusion, abatement programs should include resources devoted to addressing the substantial minority of individuals with non-medical opioid use. Clinicians should be trained to routinely evaluate patients for such practices, PDMP data should be increasingly integrated within health systems and electronic medical records, and interventions should be deployed to decrease the volume of opioids prescribed, which in turn will decrease the incidence of non-medical opioid use. Once non-medical opioid use has been identified, greater clinical resources should be devoted both to addressing non-medical opioid use directly as well as evaluating and treating potential contributory factors ranging from comorbid social stressors or mental illness to untreated or undertreated chronic pain syndromes.

CONFIDENTIAL

D. MANAGING COMPLICATIONS ATTRIBUTABLE TO THE EPIDEMIC

The goal of this abatement remedy is to provide unfettered access to high quality, longitudinal, compassionate, and comprehensive treatment to individuals with OUD who have complications from the disorder. Such complications include chronic infectious diseases, such as hepatitis C (HCV) or HIV, acquired through the sharing of needles during injection drug use, as well as endocarditis and valvular heart disease, complications from blood-borne bacterial infections that can seed the heart valves and cause significant morbidity and mortality.

121. An estimated 4.1 million people in the U.S. are infected with HCV⁴¹⁰ and 1.1 million are infected with HIV, with about 25% of HIV cases co-infected with HCV.^{411, 412} Individuals that are co-infected with HIV and HCV have a greater risk for chronic liver disease and liver-related death than individuals living with HIV alone. While studies suggest only a small proportion of individuals with non-medical opioid use progress to heroin,⁴¹³ there are nevertheless millions of individuals who report such non-medical opioid use in the United States. Injection drug use (IDU) is a primary risk factor for the acquisition and transmission of both HCV and HIV, and the opioid epidemic has resulted in a sharp increase in both of these diseases. From 2009 to 2018, the CDC estimated the number of acute HCV cases increased threefold,⁴¹⁴ and states with the highest rate of new HCV infections, such as West Virginia, Kentucky, and Tennessee, were also among those that have been hardest hit by the opioid epidemic.⁴¹⁵ Several studies have reported significant associations between the opioid epidemic and HCV.^{416,417}
122. One example of a microcosm illustrating the interconnectedness of the opioid epidemic and HIV and HCV infections was seen in rural Scott County, Indiana. In 2015, this rural county experienced a community outbreak of HIV, and by April 2016, there were 188 confirmed cases of HIV infection, of which 92% were coinfecting with HCV.⁴¹⁸ The Indiana State Department of Health led an investigation into this outbreak and determined it to be linked to the injection of the prescription opioid oxycodone.⁴¹⁹ This outbreak also highlighted the vulnerabilities of communities to handle these crises.^x
123. Individuals with OUD should be targeted for HCV and HIV screening and referral, since the effectiveness and cost-effectiveness⁴²⁰ of screening for HCV and HIV is well-established. There are many opportunities for screening individuals with OUD, including at EDs, residential or outpatient treatment facilities, SSPs, and jails and prisons. In particular, efforts should be focused on screening individuals who inject drugs and share injection equipment. The CDC recommends such individuals be tested for HIV annually;⁴²¹ HCV screening should also be performed annually and jointly with HIV screening,⁴²² allowing for the effective use of existing infrastructure and resources to address both diseases. Additionally, integrating HCV and HIV testing and counseling programs may reinforce prevention education messages to reduce risky behavior among high-risk populations such as PWID.⁴²³
124. It is crucial that HCV and HIV screening is effectively linked to post-test services and support including treatment and counseling, since the performance of screening without proper and effective

^x Of note, NIDA cites the implementation of a syringe services program as a major factor helping to bring this HIV outbreak under control. (Available at: <https://www.drugabuse.gov/about-nida/noras-blog/2016/12/syringe-exchange-programs-are-part-effective-hiv-prevention>)

CONFIDENTIAL

referral channels could lead individuals to miss out on timely initiation of prophylaxis and treatment, which may accelerate disease progression and lead to an increased transmission rate within the community. The safety and effectiveness of HCV treatment has improved markedly during the past few years with several new FDA-approved medications. Current HCV treatments usually require just 8 to 12 weeks of oral therapy and can cure over 90% of patients with few side effects.⁴²⁴ Early HCV treatment helps to prevent or limit the development of cirrhosis, lowering the risk of developing liver cancer, liver failure, and other complications, in addition to limiting the risk of HCV transmission to sexual partners or children, increasing survival, and improving quality of life.⁴²⁵ As a result, HCV treatment is cost-effective.^{426,427} A longitudinal, community-based cohort study of 1,323 participants who had chronic HCV at baseline, found that 52% of the cohort had undetectable HCV RNA.⁴²⁸ This study also found that individuals with undetectable HCV RNA were half as likely to die and had a four-times lower odds of cirrhosis compared to individuals with detectable HCV RNA.⁴²⁹ Additionally, patients can be re-infected with HCV, reinforcing the need for SSPs to be easily accessible to prevent the spread of HCV.

125. Timely HIV treatment is also important as it significantly improves survival and quality of life, limits HIV transmission, and slows the progression of the disease.⁴³⁰ HIV is a chronic condition that currently requires lifelong treatment and monitoring and, as a result, continued treatment services are critical as lapses in care could lead to suboptimal outcomes and continued HIV transmission.⁴³¹
126. Endocarditis is another rare but serious complication of OUD and has long been regarded as one of the major causes of morbidity and mortality among those who inject drugs.⁴³² Infective endocarditis (IE), or infection and inflammation of the heart valves and lining of the heart chambers, is caused by bacteria entering the blood stream and attacking heart valves. Acute endocarditis is especially severe and common among PWID and often results in additional infection, or septic emboli, of the kidneys, lungs, and brain.⁴³³ In one report, hospitalizations for endocarditis increased twelve-times among individuals with drug dependence in North Carolina between 2010 to 2015; one-third of these individuals were infected with HCV and the average cost of each hospitalization exceeded \$50,000.⁴³⁴ In another report using the Health Care and Utilization Project National Inpatient Sample (HCUP-NIS), the proportion of national IE-related hospitalizations that were attributable to IVDU increased from 7.0 to 12.1% between 2000 and 2013, which the authors noted “appear to mirror those of the intertwined prescription opioid, heroin, HCV, and overdose epidemics throughout the country.”⁴³⁵ These findings are important because of the morbidity associated with the disease, with estimates of in-hospital mortality as high as 11 to 26% and 5-year mortality as high as 12 to 50%.^{436,437,438}
127. Compared to IE patients that did not inject drugs, PWID with IE have a significantly higher likelihood of open cardiac surgery, longer hospital stays, and nearly 1.5-times higher hospital costs.⁴³⁹ Additionally, a study from Boston, Massachusetts found that despite PWID being younger and having fewer cardiovascular risk factors than non-PWID with IE, PWID patients had nearly a four-times higher risk of valve-related complications.⁴⁴⁰ Among individuals with IE involving the right side of the heart, injection drug use was noted among approximately one-third (29.5%) of individuals in a literature review of 262 individuals from 2008 to 2013.⁴⁴¹ One nationwide study found the overall incidence rate of IE associated with IVDU increased over 250% between 2009 (30 per 10,000 cases) and 2016 (79 per 10,000 cases).⁴⁴² Another study found a 436% increase in IE cases associated with IVDU, from 33 to 177 between 2012 and 2017.^{443,444} The majority of these cases were due to heroin

CONFIDENTIAL

IVDU. Nearly half (49%) of the patients were re-hospitalized and 40% relapsed; between 2012 and 2017, the death rate increased from 9% to 25%.⁴⁴⁵

128. Endocarditis treatment initially requires inpatient hospitalization and intravenous antibiotic administration. In some cases, the damage to the heart valve is so severe that it must be replaced surgically. Unfortunately, complications such as lack of response to antibiotics or embolization that causes strokes may occur, and also prove fatal. These cases pose a high burden on hospitals in local communities because of their social and clinical complexity and because of the very high risk of rehospitalization if IVDU is not discontinued. However, hospitalization represents an opportunity for delivery of addiction counseling, enrollment in treatment, and education on harm reduction strategies. In a retrospective study of patients hospitalized for injection drug use-associated IE in Massachusetts between 2011 to 2015, patients were examined for receipt of MAT within three months after hospital discharge. Receipt of MAT was associated with reduced mortality in the month that MAT was received.⁴⁴⁶
129. Many barriers will have to be overcome to consistently provide high quality, longitudinal, compassionate, and comprehensive treatment to individuals with complications from OUD such as those described above. For example, one study surveyed 333 patients living with HIV between 2007 and 2008 to examine barriers to support service use and factors associated with need and unmet need for services.⁴⁴⁷ The analysis found that 71% of patients reported needing at least one supportive service. Barriers to accessing such services included lack of information (47% reported not knowing where to go or who to call); administrative burdens (33% reported the system too confusing and/or the wait list too long); and financial or logistical barriers (18% reported treatment too expensive and/or transportation problems). A survey of individuals with HCV, including some also with HIV, between November 2013 and July 2015, found that over 93% of participants wanted HCV treatment but approximately half were unable to spend anything out of pocket for their treatment.⁴⁴⁸ In addition to cost, participants also reported that access to medications and provider reluctance delayed treatment initiation.
130. In conclusion, the opioid epidemic has had many ripple effects, and transmission of HIV and HCV among people who use drugs has flourished due to increases in the number of individuals with OUD. Fortunately, HIV and HCV are well understood diseases, and effective treatments, and in the case of HCV, curable ones, exist. Many barriers must be overcome to achieve the widespread screening and treatment that is required to abate these elements of the opioid epidemic in the U.S., and individuals with other costly and complex sequela of the epidemic, such as infectious endocarditis, also require special clinical care, coordination, and support. As with other programs proposed in my abatement plan, these components have a favorable return on investment and will help individuals avoid preventable adverse events related to these infectious diseases.

CONFIDENTIAL

E. WORKFORCE EXPANSION AND RESILIENCY

The goal of this remedy is to expand the healthcare workforce, since local communities benefit from well-trained healthcare professionals who are equipped to deliver services for those living with chronic pain and/or OUD. The workforce must be trained and equipped to meet the needs of these individuals, and to provide evidence-informed services to address the social and medical harms associated with the opioid epidemic.

131. Workforce assessment. Given the scope of the challenge, efforts to expand workforce capacity in local communities should consider a systematic workforce assessment to determine gaps in the available supply and core competencies of the clinical and social service workforce available to address the opioid epidemic. Such an assessment should explore the available supply of managerial and administrative professionals, nurse and medical practice leaders, social workers and case managers, recovery coaches and paraprofessionals available to assist people with OUD. Such evaluations should include assessments of the workforce's core technical and cultural competencies regarding pertinent OUD treatment and service interventions.
132. Recruitment and Retention. Given the safety and efficacy of MAT to treat OUD, some efforts have focused on increasing the number of OUD treatment providers. For example, Massachusetts General Hospital launched a three month "Get Waivered" campaign which resulted in 95% of its general emergency medicine physicians successfully completing the eight-hour training course required to earn a DEA buprenorphine waiver.⁴⁴⁹
133. While in April 2021, the Biden-Harris Administration announced that prescribers would no longer have to complete an eight-hour training program prior to prescribing buprenorphine for OUD, prescribers are still required to submit a letter to SAMHSA that they intend to prescribe it, and many structural barriers to increasing the use of buprenorphine remain.⁴⁵⁰ For example, across the U.S., many providers do not prescribe buprenorphine to their maximum patient limit. Measures to address known organizational barriers and to improve provider confidence and expertise in addressing addiction may be helpful in addressing these challenges. For example, some communities have found success in establishing comprehensive clinics where community providers can dedicate time to seeing patients for addiction treatment that is distinct and separate from their regular practice.⁴⁵¹ Although such an effort continues to segregate addiction care, in some settings it has increased provider capacity and given support to health care professionals. Greater deployment of nurse practitioners with primary care expertise may also help to expand patient access to MAT.⁴⁵²
134. Medical Social Workers. Medical social workers address the psychosocial needs of an individual, such as housing or transportation, that increase the likelihood of continuing treatment and recovery. Social workers should be integrated within the continuum of medical care for OUD to utilize community resources and ensure wraparound care. The intensity of social work intervention will vary based on the needs of the population and duration that they have been in care. For example, pregnant women who are newly linked to treatment will require more intensive social work and case management services, which can be tapered down after two-years in care (see Section 4A). Additionally, social workers are also effective in services for families and children (Section 4C), homeless individuals and those who are housing insecure (Section 4F), reentry and reintegration programs (Section 3B), and for individuals newly entering OUD treatment (Section 2B). Expanding

CONFIDENTIAL

case management to these populations would ensure that individuals will not “fall through the cracks”, improving treatment and recovery outcomes.

135. Care coordination. As health care has become more specialized and fragmented, social work case managers and support staff are also needed to coordinate care and facilitate communication between members of the health team. This is important both for the treatment of OUD and for preventing non-medical opioid use among patients treated for pain. In addition to ensuring smooth transitions between different levels of care, case managers can assist clients in setting treatment goals. One community-based, behavioral intervention trial found that compared to passive referral, individuals who received case management were 50% more likely to engage in treatment with MAT within seven days.⁴⁵³
136. Primary care workforce. In addition to expanding OUD treatment capacity, national abatement efforts should also invest in expanding and developing a support infrastructure for the general primary care workforce, given the many varied personnel involved in the care and management of patients with OUD.⁴⁵⁴ Individuals with OUD have a high burden of chronic health care conditions that require ongoing treatment from health care providers.^{455,456} It is important that infrastructure to support health providers delivering primary care also be expanded. Any health system’s treatment capacity is also reliant on administrative and support personnel. For example, insufficient administrative support has been identified as a common barrier in prescribing buprenorphine in ambulatory settings.⁴⁵⁷
137. Addiction counselors and physician specialists. Any workforce assessment can also help to evaluate the level of community need for addiction counselors and physician specialists, who may specialize in underserved, yet vital specialties such as, addiction treatment, pain, or child and adolescent psychiatry. For example, addiction physician specialists are well-versed in addiction medicine and/or integrative care that combines pharmacologic and non-pharmacologic treatments for pain. Fellowships can be leveraged to facilitate such specialized training. Fellowships are typically one-year ambulatory programs that allow fellows to obtain and demonstrate competence in patient care in a given clinical area. For addiction physician specialists, they receive additional training in the diagnosis, management, and treatment of the spectrum of unhealthy substance use and addiction.⁴⁵⁸ Similarly, pain specialists should gain familiarity and experience on different acute and chronic pain management options.
138. Specialized clinical pharmacists. Medications for addiction treatment are highly effective for many individuals with OUD and reduce the likelihood of opioid-related morbidity and mortality (see Section 2B). Given the importance of appropriately managing MAT, research has demonstrated the benefit to integrating specialized clinical pharmacists into teams providing OUD treatment.^{459,460} Not only may pharmacists promote the safety and appropriate use of medications, they can administer or provide directly observed treatment for MAT, and consult with both prescribers and patients.⁴⁶¹ In one local community, specialized behavioral health pharmacists are expanding into community clinics in order to support comprehensive treatment and medication management.⁴⁶²
139. Medical examiners. Medical examiner data is crucial for overdose mortality surveillance.⁴⁶³ However, medical examiners must work within the constraints of their operating budget, and as observed in other states heavily hit by the opioid epidemic, the increasing number of overdose deaths has strained medical examiner offices.^{464,465} As such, local communities may consider expanding

CONFIDENTIAL

support for medical examiners in order to alleviate the strain caused by the increasing number of opioid-related deaths and increasing complexity of toxicology testing due to synthetic opioids.

140. Opioid stewardship programs. During the past decade, health systems have increasingly relied upon opioid stewardship programs as a means to gain control of the opioid epidemic and its deleterious impact on their patients and programs.⁴⁶⁶ Similar to antibiotic stewardship programs that have flourished because of widespread overuse and misuse of antibiotics, the concept of opioid stewardship recognizes that opioids can provide value when used in accordance with the best evidence, but that they have been widely used in settings with an unfavorable risk/benefit balance. Stewardship programs require strong executive sponsorship and collaborative efforts from stakeholders and they provide a framework to develop, implement and continually evaluate policies governing the use of opioids in clinical practice. Typically, an opioid stewardship committee would be responsible for conceptualizing, designing, implementing, and evaluating surveillance and initiatives to ensure optimal opioid use, such as a program to improve the rates of buprenorphine induction in the ED, or to increase the delivery of non-pharmacologic care for those with complex chronic pain.⁴⁶⁷ Such committees typically include representatives from various departments including but not limited to: anesthesiology, nursing, psychiatry, ambulatory medicine, pain medicine, medical education, surgery, and community health.
141. Compassion fatigue and workforce resiliency. Compassion fatigue has been referred to as the “cost of caring” with symptoms that mirror post-traumatic stress disorder.⁴⁶⁸ Repeated exposure to traumatic experiences, such as multiple overdoses and overdose-related deaths among young people, impact emergency responders emotionally, behaviorally, interpersonally, and physically. Compassion fatigue and burnout result in increased turnover and decreased empathy. A survey of behavioral health and emergency preparedness responders found that nearly three in four (72%) were at risk of compassion fatigue and nearly one in five (19%) were at risk of burnout.⁴⁶⁹ Importantly, fewer than one in four (22%) had high resilience, which is associated with decreased likelihood of compassion fatigue and burnout. Programs to build resilience, self-efficacy, and a supportive social network among first responders are crucial to promoting a safe and healthy community. In West Virginia, the City of Huntington’s Compass project serves as one such program; it focuses on developing tools and a foundation to cope with high-stress situations, such as self-care skills, wellness resources, and nutrition and exercise.⁴⁷⁰ A literature review of 25 studies assessing interventions to reduce burnout found that a combination of person-level (e.g., mindfulness, self-care, coping) and organization-directed interventions (e.g., professional support systems or “buddy systems”, workplace policies) found positive effects and reduced burnout lasted for at least one year, whereas the positive effects of person-level interventions alone lasted for only six-months.⁴⁷¹
142. Healthcare is a labor-intensive field, and investment in a qualified and engaged multi-disciplinary workforce is foundational, yet there has often been a lack of discourse regarding the human resources and capital needed to address the opioid epidemic. There are three major components to an expanded health care professional and paraprofessional workforce: (1) conducting a workforce assessment to determine key staff and training needs in local communities; (2) expanding the number of OUD treatment providers, medical social workers, primary care providers, addiction counselors, physician specialists, medical examiners and other specialists equipped to address the opioid epidemic; and (3) creating and expanding programs that address burnout/compassion fatigue. Medical social workers should be expanded and incorporated into clinical settings across the U.S., where they can assist in

CONFIDENTIAL

linking individuals to treatment and community resources. Additional social workers, case managers, and support staff should be implemented across communities to provide care coordination between chronic care, behavioral health care, OUD treatment, and other services. Specialized clinical pharmacists are also necessary to provide direct observed therapy for MAT and consult patients who have questions regarding medications. In order to maintain the workforce resiliency, compassion fatigue programs should be made available for first responders and professionals whose clients have OUD or are affected by the opioid epidemic such as nurse practitioners. Opioid stewardship programs should be implemented to improve the quality care for individuals in clinical settings.

143. In conclusion, an effective response to the opioid epidemic must include investments in the nation's healthcare workforce to address prevention as well as evidence-based pain and OUD treatment. The workforce must include recruitment and retention of OUD treatment providers, social workers, care coordinators, primary care workforce, addiction counselors, physician specialists, and medical examiners in order to provide comprehensive healthcare and wraparound services that address the medical and psychosocial needs of individuals with OUD and their families. Finally, programs should be supported and deployed to ensure the resiliency of the current and future workforce, and opioid stewardship to improve the quality care of patients in clinical settings.

CONFIDENTIAL

F. DISTRIBUTING NALOXONE AND PROVIDING TRAINING

The goal of this remedy is to expand upon and support the efforts of the naloxone distribution and training in the U.S. This is important because naloxone is an opioid antagonist, or "blocker", that can save lives by safely and rapidly reversing opioid overdoses. However, its costs, stigma, and other barriers have historically limited accessibility to those in need.

144. Naloxone works by binding to opioid receptors and blocking respiratory depression and other effects of prescription opioids and heroin, or illicit fentanyl, if someone has opioids in their system. It comes in three FDA-approved formulations: injectable, autoinjector delivered, and nasal spray ("Narcan"). Though injectable naloxone is the least expensive, use of the injectable formulation requires professional training.
145. Naloxone is a non-scheduled prescription medicine rather than a controlled substance, and there is widespread consensus that naloxone distribution and training represent an important method to reduce opioid-related overdose.⁴⁷² In a randomized controlled trial, intranasal naloxone reversed heroin overdose successfully in 82% of patients,⁴⁷³ and naloxone distribution and training programs have also shown over 80% effectiveness at reversing overdoses in community settings.^{474, 475} In a systematic review of take-home naloxone programs for individuals likely to witness an opioid overdose, naloxone was associated with successful overdose reversals in 96.3% of the patients (2,249 successful overdose reversals among 2,336 administrations).⁴⁷⁶ It is important to note that there is no evidence to support the notion that naloxone use encourages and enables drug use.^{477, 478}
146. There are several key populations who will benefit from access to naloxone. These include: individuals who have recently overdosed; individuals who are maintained on chronic, high-dose opioids; individuals with OUD; and individuals recently released from incarceration. For example, a study in North Carolina examined the difference in opioid overdose death rates between former inmates and general residents found that former inmates were 40 times more likely to die of an opioid overdose than someone in the general population.⁴⁷⁹
147. Many other community-level evaluations have been performed. For example, a study of 19 geographically distinct cities and towns in Massachusetts found that opioid overdose death rates were 27% to 46% lower in communities where overdose education and naloxone distribution had been implemented.⁴⁸⁰ A study of a naloxone distribution program in North Carolina suggested that counties in the state that distributed naloxone kits had a 10% to 12% lower opioid overdose death rates compared to their counterparts, avoiding 352 overdose deaths between 2013 to 2016. A population-based study published in May 2019 that analyzed data from the 2005-2016 National Vital Statistics System found that states that allow direct dispensing of naloxone by pharmacists (or, "direct authority") were associated with a significantly reduced rate of fatal opioid-overdoses.⁴⁸¹ Public lock boxes containing naloxone have been implemented in Rhode Island and Ohio, and are one method to ensure community access of naloxone where overdoses may frequently occur (e.g., libraries).⁴⁸² These are similar to boxes with automated external defibrillators (AEDs) that are routinely available in movie theaters, malls, schools, airports, and houses of worship.
148. Despite its benefits, naloxone distribution and training will have a finite impact on the opioid epidemic. Not all overdoses are witnessed by someone willing and able to administer naloxone. In addition, the long-term public health impact of naloxone programs depends on what happens after an

CONFIDENTIAL

overdose is successfully reversed.⁴⁸³ For example, successfully revived individuals remain vulnerable to future overdose and death, and individuals who overdose once have escalating risks of future overdoses. After naloxone, individuals may temporarily or permanently abstain from use, continue as active users, obtain addiction treatment, overdose again, or die of other causes. Naloxone distribution must be accompanied by direct training, and its role in reversing overdoses should also be considered for inclusion in educational campaigns. Ultimately, the outcomes of an overdose reversal depend upon the availability and comprehensiveness of OUD treatment, other mortality risks, and background factors. These factors underscore the importance of a comprehensive abatement approach.

149. In conclusion, efforts to support naloxone distribution, training, and use can be categorized in several distinct channels.^y First, first responders, such as law enforcement officers, firefighters, and paramedics and emergency medical technicians (EMTs), should be provided with naloxone and training, since these individuals often serve as the initial point of contact with those who have overdosed. Second, EDs across local communities should have sufficient naloxone doses for hospitalized overdose cases and doses to expand access to take-home naloxone once patients are discharged. Third, high-risk patients, such as those who are maintained on chronic, high-dose prescription opioids or who have already experienced a non-fatal overdose, should be prescribed naloxone and trained on how to administer it. Such individuals can be reached through ambulatory and community-based programs, or on follow up visits after an overdose. In many cases, such training should also include their social network, caregivers, and/or family members, given the likelihood that these individuals would be most likely to respond to an overdose. Another group of high-risk individuals who should receive naloxone are individuals who have OUD and were recently incarcerated, as well as upon release from incarceration. Finally, naloxone should be distributed throughout communities in public lock boxes to improve the capacity of bystander rescuers to save the lives of opioid overdose victims.

^y Additional formulations and continued innovation in the naloxone market are likely, and abatement remedies should remain flexible to keep pace. For example, in April 2021 the FDA approved a new, higher naloxone dose, and new naloxone formulations may be developed over the coming years that have significant advantages over currently available formulations.

CONFIDENTIAL

CATEGORY 3: RECOVERY – ENHANCING PUBLIC SAFETY AND REINTEGRATION

This category of my abatement plan seeks to improve public safety and support individuals currently in recovery from OUD. Recovery from OUD and the complications associated with OUD must be accompanied measures to reintegrate individuals back into the community.

A. PUBLIC SAFETY

Law enforcement officers are in a key position to help reverse the opioid epidemic across local communities as they respond to overdoses and engage in public health oriented policing interventions. Despite this, police departments, as with other local agencies, have been stretched thin because of the demands of the opioid epidemic, diminishing their ability to address other public safety needs. The abatement interventions proposed in this report, combined with the expansion of social workers and mental health personnel, will address or prevent many of the calls that police and other first responders currently respond to. However, in addition to expansion of treatment and mental health services, there is also a need for stigma reduction training and pretrial diversion of select non-violent offenders with active OUD, as well as a greater number of specialized detectives who can focus on disrupting opioid trafficking networks.

150. Training to reduce stigma. Since law enforcement officers are often the first responders to an overdose, it is important to provide law enforcement with the training and confidence to appropriately respond.^z While not focused on opioid overdose per se, Crisis Intervention Team (CIT) training for officers to reduce stigma related to behavioral health crises has been effective at improving officers' attitudes toward individuals with mental health issues^{484,485} and self-efficacy in handling these calls.^{486,487} Such training has also reduced arrests and use of force,⁴⁸⁸ and increased referrals for services during a mental or behavioral health crisis.^{489,490} Such training, which should be repeated at regular intervals, may reduce stigma by law enforcement towards people with OUD, increase the likelihood that individuals will call 911 for help, and improve referrals for services and/or treatment.

151. Pretrial Diversion. Pretrial diversion, sometimes referred to as Law Enforcement Assisted Diversion (LEAD), offers eligible individuals who would otherwise be arrested for drug-related charges the opportunity to instead access community-based services and/or treatment.⁴⁹¹ These programs are unique in that they occur pre-booking so that if an individual who qualifies for the program chooses to enroll, they do not have an arrest on their record if they complete program requirements. Qualifications are typically based on having committed a low-level drug offense and factors such as the amount of drugs possessed, absence of any intent to distribute, absence of disqualifying criminal history such as violent crime, and are determined by a social worker/mental health professional that is embedded in the police department.⁴⁹² Thus, in contrast to drug courts, LEAD participants never enter the criminal justice system and they are enrolled in the program instead of being charged with a crime. Diversion programs reflect partnerships between law enforcement and local behavioral health systems to enroll individuals in appropriate services.^{aa} LEAD pretrial jail diversion programs

^z Law enforcement officers within prisons and detention centers should also undergo similar training, given high rates of stigma in these settings as well.

^{aa} Such programs extend and formalize informal diversion that may take place when, for example, law enforcement bring an individual who overdosed to an Emergency Department rather than detention facility for evaluation, treatment and referral to treatment.

CONFIDENTIAL

are designed to expedite treatment for individuals with substance use disorders while reducing strain on the criminal justice system.

152. Seattle created the first LEAD program and evaluations suggest improved outcomes for participants including housing, employment, and reduced recidivism.^{493,494} For example, LEAD participants with suspected low-level drug offenses had fewer arrests and felony charges, shorter jail time, and less interaction with the legal and judicial system.^{495,496} Additionally, participants were twice as likely to have been sheltered, 90% more likely to have permanent housing, and almost half were either employed or in vocational training.⁴⁹⁷ LEAD programs modeled after Seattle's experience have since been successfully implemented in other jurisdictions.⁴⁹⁸ LEAD programs are an important means of reducing the rate of individuals with low-level drug offenses entering prison and addressing environmental factors that contribute to repeat offenses among individuals with OUD.⁴⁹⁹ As with CIT, law enforcement officers require training that should be repeated at regular intervals to maximize their familiarity and expertise with the conduct of LEAD.
153. Specialized opioid units. Some police departments have created specialized units to address the opioid epidemic. These units are often comprised of detectives, sometimes within homicide or narcotics units, who work to link together overdose incidents across the city by identifying similar contacts, sources, dealers, or other features between overdose events. These units treat sites of overdoses as crime scenes and work to track back to dealers and build cases for prosecution to bring down higher level supply sources for opioids.⁵⁰⁰ The optimal specific size and composition of these units, as with other components of an effective law enforcement response to the epidemic, will depend upon many features of the local community, including the size and urbanicity of the jurisdiction as well as the burden of prescription opioids, heroin, and illicit fentanyl.
154. In conclusion, law enforcement plays a vital role in an effective public safety response to the opioid epidemic, and abatement programs across the U.S. should include resources to support a variety of different functions. LEAD programs may be used by police departments to divert as many qualified individuals as possible. Additionally, specialized overdose units may be used to investigate and disrupt higher-level opioid trafficking. Finally, it is important that police and correctional officers receive continuous stigma reduction training, so they are better prepared when interacting with individuals with OUD or who have overdosed.

CONFIDENTIAL

B. CRIMINAL JUSTICE SYSTEM

The criminal justice system is a major thoroughfare for individuals with opioid addiction and represents an opportunity to identify and link those individuals to treatment, reducing their risk of overdose and recidivism while improving their societal reintegration. This remedy also focuses on ways that the criminal justice system can positively impact the opioid epidemic, such as the provision of drug courts, universal screening upon booking, MAT, reentry programs, and transitional housing for those with OUD who are newly released and in need of housing.

155. The opioid epidemic has burdened the U.S. criminal justice system with a surge of inmates, increasing health care costs associated with OUD and producing high rates of overdose and recidivism. Data from the Department of Justice suggest over half of the incarcerated population nationwide has a substance use disorder,⁵⁰¹ approximately one in four state prisoners nationwide between 2007-2009 reported prior heroin or opioid use,⁵⁰² and by some estimates, as many as one-fourth to one-third of individuals with heroin addiction are estimated to pass through the criminal justice system each year.⁵⁰³
156. Drug courts. There is substantial evidence regarding the role that drug courts can play in diverting non-violent offenders from the criminal justice system to the treatment system, where their needs can be more effectively addressed.⁵⁰⁴ These programs represent special court dockets that provide judicially-supervised substance use treatment in lieu of incarcerating individuals with drug-related offenses. The President's Commission on Combating Drug Addiction and the Opioid Crisis included a recommendation that the "DOJ [Department of Justice] broadly establish federal drug courts within the federal district court system in all 93 federal judicial districts." Further, the Commission reported "States, local units of government, and Indian tribal governments should apply for drug court grants established by 34 U.S.C. § 10611. Individuals with a [substance use disorder] who violate probation terms with substance use should be diverted into drug court, rather than prison."⁵⁰⁵
157. One of several sources of evidence to support the efficacy of drug courts is a comprehensive review published in 2011 by the U.S. Department of Justice that examined drug courts in the U.S.; the report, which was also supported by the Office of National Drug Control Policy (ONDCP) of the Executive Office of the President, found that the combination of comprehensive treatment services and individualized care provided by drug courts is an effective way to provide treatment to criminal offenders with substance use disorders.⁵⁰⁶ A study conducted by the U.S. Department of Justice, published in 2020, found that drug court participants reported less drug use, lower rates of positive drug tests, and fewer rearrests than comparable offenders who did not participate in drug courts.⁵⁰⁷ Though treatment investment costs are higher for individuals participating in drug courts, the reduced recidivism resulted in an average savings of \$5,680 to \$6,208 per offender. Additionally, a 2012 meta-analysis of 154 studies found that adult drug courts reduced drug-related recidivism from 50% to 37%.⁵⁰⁸
158. Universal screening upon intake. It is important that individuals who enter jail or prison receive screening for OUD so that they may receive adequate treatment and services. Screening and in-depth assessment are important first steps in the substance abuse treatment process and an effective screening and assessment approach will encourage referral of offenders to the appropriate level of treatment.⁵⁰⁹ Assessment for substance abuse treatment in criminal justice setting should include

CONFIDENTIAL

substance abuse history, psychopathy and related risk factors, history of mental health problems, and other psychosocial areas that are affected by substance abuse.

159. MAT treatment. Nationally, fewer than 20% of individuals with substance use disorders in the criminal justice system receive treatment,⁵¹⁰ and what treatment is received is often inadequate. According to the Federal Bureau of Justice Assistance, as of August 2017, only 30 of the 5,100 (0.6%) prisons and jails in the U.S. offered opioid users methadone or buprenorphine,⁵¹¹ despite evidence that such treatment improves treatment entry and retention after release if arrangements exist to continue treatment.⁵¹² Because of this, induction facilities and access to MAT, as well as other treatments along the continuum of care, are important for those incarcerated in jails, prisons, or juvenile detention facilities.⁵¹³ A systematic review and meta-analysis found that MAT was associated with a lower risk of all-cause mortality and drug-related death during incarceration, following incarceration, and in other key states of the OUD population.⁵¹⁴ While MAT should be made available to anyone with OUD, such treatments are especially important for high priority populations such as pregnant women with OUD and individuals already on MAT prior to incarceration.⁵¹⁵
160. Reentry programs. Individuals released from prisons and jails face a multitude of issues that make their reintegration into the community challenging, including substance use or mental health problems and having no or little qualifications and skills that make them employable.^{516,517} To address this issue, many jurisdictions in the U.S. have developed and implemented reentry programs that include substance use treatment, mental health services, transitional housing, education and job readiness assistance, and employment services.^{518,519} A study of young offenders aged 16 to 25 years enrolled in the Substance Use Treatment and Reentry (STAR) Program in Los Angeles found that over 70% were still employed a year after initiating the program, self-reported arrests were below 15%, and there was a reduction in substance abuse among participants that reported drug use at intake.⁵²⁰ A study of Florida inmates between January 2006 and December 2008 found that reentry and transitional substance use programs had some of the largest effects on increasing employment and reducing recidivism.⁵²¹ In 2018, the Council of State Governments Justice Center, sponsored by the U.S. Department of Justice, released guidelines for “Best Practices for Successful Reentry for People Who Have Opioid Addictions” that describe efforts local agencies can implement to ensure successful reentry.⁵²² Successful reentry programs must simultaneously assess the need for, and deliver to participants, supportive services and programs across a number of dimensions, including housing, education, employment, health and well-being, and family reunification and support.⁵²³
161. Transitional housing. Securing housing is one of the most immediate challenges facing prisons upon their release. Housing options are extremely limited for newly released individuals who do not stay with family or friends, and obtaining housing can be complicated by a host of variables including scarcity of affordable housing, prejudice that restrict tenancy, and strict eligibility requirements for federally subsidized housing.⁵²⁴ According to an analysis of almost 18,000 previously incarcerated adult respondents to the 2008 National Former Prisoner Survey, formerly incarcerated individuals are almost 10 times more likely to be homeless than the general public.⁵²⁵
162. In conclusion, a large proportion of individuals with OUD, or who have otherwise been impacted by the opioid epidemic, come into contact with the criminal justice system each year. Because of this, as well as the demonstrated benefit of interventions such as those identified above, many further

CONFIDENTIAL

investments are needed. For these efforts to be successful, the Courts must be equipped with a sufficient number of court dockets, support staff, and wraparound services including social workers and case managers. Additionally, all individuals (re)entering the criminal justice system should be screened for OUD and individuals who need treatment must receive appropriate care, including MAT, while incarcerated. Inmates released while still receiving treatment should be closely linked to agencies and organizations that provide treatment upon reentry to avoid lapses in treatment and suboptimal treatment outcomes. Moreover, individuals with OUD released from jails or prisons should be linked to existing reentry programs that provide transitional housing for those who are at a high risk of homelessness, social services, and jobs/vocational training. Such investments will not only be of direct benefit to the participating individuals, but also of broader societal benefit as they strengthen families, enhance community reintegration, and help local areas hard hit by the epidemic to recover.

CONFIDENTIAL

C. VOCATIONAL TRAINING

The goal of this remedy is to promote economic development to make gainful employment readily available to individuals with OUD or who have been otherwise impacted by the opioid epidemic. This is important because of the complex but beneficial relationship between employment and recovery.⁵²⁶

163. Jobs training and placement services for individuals with OUD. The opioid epidemic has been particularly profound in many parts of America that have simultaneously experienced significant economic decline. While the relationship between economic hardship and opioid morbidity and mortality is complex,^{527,528} there is widespread consensus that jobs training is important for under- and unemployed individuals with OUD.⁵²⁹ Unemployment is a significant risk factor for substance use and relapse, and OUD is itself a significant employment barrier, yet not⁵³⁰ a qualifying condition for federal disability programs.^{531,532} Many people living with OUD face other employment barriers, including educational challenges⁵³³ and co-occurring physical or mental health challenges, that may be addressed in vocational services, including those offered within addiction treatment.⁵³⁴ For these reasons, comprehensive treatment programs, as well as diversion and reentry programs, often include vocational training and job placement. It is important that vocational training programs incorporate pre-employment preparation, gradually increasing hours and work responsibility, and ongoing support from counselors and peers.⁵³⁵ Existing data suggest that vocational services within substance use disorder treatment are cost-effective,⁵³⁶ though such programs face many barriers in creating successful paths to employment. Trials are now underway to explore the effectiveness of alternative models.⁵³⁷

164. Recovery-supportive workplaces. Incorporating peer support and case management services, or mentor support within workplaces, have been linked to successful workplace reintegration.⁵³⁸ Employers can foster workplace environments that welcome individuals in recovery, and that seek to reduce addiction stigma.⁵³⁹ Employers can anticipate and address predictable challenges employees may face. For example, they can make available onsite or telehealth counseling for both scheduled and on-demand recovery support. To reduce both absenteeism and missed appointments, employers can facilitate peer support groups designed around workers' daily schedules. Work sites can openly support MAT and ensure that health plans comply with the letter and spirit of mental health and addiction parity requirements which are intended to ensure proper access to Suboxone and other therapies.⁵⁴⁰ Other measures, such as incorporating vocational rehabilitation counselors (i.e., peer support specialists or case managers) can help ensure support for both workers and employers.⁵⁴¹

165. Accountability and safety measures. To be effective and sustainable, public workplace policies must address the needs and preferences of local employers. Such measures may include policies to promote drug- and alcohol-free workplaces. Accountability measures within recovery-supportive workplaces sometimes include drug testing and other measures to ensure safety in specific roles such as those involving operating heavy machinery. Although such policies might appear to disadvantage people with experience of OUD, evidence-based, transparent policies that address safety⁵⁴² and productivity concerns lessen employers' incentives to implicitly or explicitly discriminate against job applicants and workers on the basis of substance use disorders.

166. Individualized employment supports. Many people living with OUD and co-occurring mental illness experience particularly severe employment barriers. These individuals may benefit from Individual Placement and Support (IPS) models that include individualized long-term supports. A strong body

CONFIDENTIAL

of research supports the effectiveness of IPS in assisting individuals with serious mental illness, many of whom have co-occurring substance use disorders, to obtain competitive employment.^{543, 544} Although the specific elements of such interventions vary, the IPS model includes several core elements, including being open to anyone who wants to work and focusing on employment within the competitive labor market rather than within a sheltered or segregated setting. To avoid the stigma of prolonged joblessness, IPS focuses on rapid job search integrated with other service interventions. Participants receive individualized long-term supports which, if necessary, are integrated with addiction or mental health treatment. Within randomized trials that compare IPS with usual interventions, IPS participants display higher employment rates and higher incomes, and appear to experience higher quality of life.⁵⁴⁵

167. Addressing obstacles to education and employment. Structural barriers exist that prohibit individuals in OUD recovery from returning to education or gaining employment. One method to address this is through the use of scholarships that help pay for school or vocational training, in conjunction with mentorship while in school. Programs to support students that are at risk of dropping out of school, who share many of the challenges experienced by students recovering from substance abuse, have proven effective. For example, two randomized controlled trials have shown that the Accelerated Study in Associate Program – through academic, personal, and financial support – is effective at improving the graduation rate among low-income students that would otherwise be at increased risk of not completing their degree.^{546,547,548}
168. Separately, “Ban the Box” is a program that addresses barriers to entering the workplace and has benefited individuals with lived experience in the criminal justice system.⁵⁴⁹ These programs prohibit prospective employers from inquiring about an applicant’s criminal history on an initial job application; the term refers to the box that individuals are sometimes asked to check on an application as to whether they have a criminal record. Across local communities, a modified version of “Ban the Box,” may balance the interests of employers and workers. For example, a community might prohibit requiring job applicants to supply information regarding arrests that do not result in convictions, misdemeanor convictions, or arrests for drug offenses that reflect personal use rather than more serious infractions.⁵⁵⁰
169. In conclusion, an effective response to the opioid epidemic must include job opportunities and vocational training for individuals with OUD. An effective jobs and vocational training program should include jobs training and placement services specifically deployed for individuals living with OUD. These evidence-based policies and programs have been shown to improve health and economic outcomes for individuals with OUD who are in recovery.

CONFIDENTIAL

D. MENTAL HEALTH AND GRIEF SUPPORT

The goal of this remedy is to ensure that mental health services, including counselling for individuals with mental illness as well as the bereaved, are available to all who may be in need. This is important because the opioid epidemic has profoundly impacted the lives of millions of individuals and their families. Factors that are intertwined with and exacerbated by the opioid epidemic, such as increased levels of death, homelessness and housing insecurity, and serious mental illness have created an unprecedented need for mental health care.

170. The opioid epidemic has resulted in a high number of deaths in communities across the U.S., which has impacted the mental health of individuals. In addition to the pain of losing a loved one, addiction and trauma further complicate the grieving process. Grief support is necessary to help bereaved family members deal with questions that may include "Why did the person die from an overdose?", "Did the person intend to die?" and "Was the death preventable?"⁵⁵¹ Death of a loved one from an overdose may be especially difficult to process because of "disenfranchised grief", resulting from lack of societal acknowledgement and support of a bereaved person's loss.⁵⁵² Such disenfranchisement may be partly driven by stigma, including attitudes ultimately internalized by the bereaved that blame the decedent or their loved ones for the death.⁵⁵³ Of course, grief is but one of many potential psychological impacts of the opioid epidemic on loved ones of those with OUD; friends and family members may also experience depression, dysthymia, anger, anxiety, post-traumatic stress, or other psychological sequela.
171. As discussed elsewhere in this report (Section 4B and Section 4C), children have also been uniquely affected by the epidemic and unfortunately, have suffered adverse psychological sequela associated with the opioid epidemic. Because of this, they too are in need of expanded, state-of-the-art mental health services. Children that have been exposed to trauma, such as parental substance abuse, separation, or death arising from the epidemic, can have difficulty in school due to problems thinking, learning, and concentrating; trust issues or difficulty forming attachment; lack of impulse control; or behavioral issues such as fighting or running away.⁵⁵⁴ Depression and anxiety also manifest differently in children than they do in adults, and may include symptoms such as irritability, changes in eating or sleep patterns, and self-injury or self-destructive behavior.⁵⁵⁵
172. Childhood trauma associated with the opioid epidemic reflects one type of adverse childhood experience (ACE), such as emotional neglect, loss of a parent, or substance abuse within the household, that increase the likelihood of subsequent mental and physical health problems.⁵⁵⁶ Specifically, ACEs disrupt neurodevelopment which results in socioemotional and cognitive impairment; this impairment results in maladaptive behaviors, such as the adoption of risky behaviors including substance abuse, and later the development of disease, disability, or social problems.⁵⁵⁷ In California, 63.5% of people have experienced at least one ACE and 17.6% have experienced four or more ACEs.⁵⁵⁸ In a study of individuals with HIV at one west coast medical center, 40% of participants reported having lived with someone with substance use issues; this was the second most common ACE.⁵⁵⁹ A 2014 study of ACEs experienced by West Virginia adults found that nearly one in three adults experienced substance use in their childhood homes.⁵⁶⁰ The same analysis reported a dose-response relationship between the number of ACEs and depression; where one-fifth of adults that had one ACE also had depression, nearly half of adults with four or more ACEs reported depression. Trauma-informed mental health care can address some of these vulnerabilities by promoting coping and adaptive behaviors key to early neurodevelopment and the prevention of future

CONFIDENTIAL

morbidity and substance use. With sufficient resources, there are programs that can use to address exposure to trauma and violence among children via the school system. For example, the Handle With Care program in West Virginia improves communication and collaboration between law enforcement, schools, and childcare agencies and mental health providers.⁵⁶¹ The program also seeks to connect families, schools, and communities to trauma-focused mental health services. In particular, social workers embedded in schools are instrumental in delivering trauma-informed counseling and wraparound services to children and adolescents in the community. Additional protective factors to address ACEs are discussed in Section 4C.

173. Addressing mental health needs within local communities is important to prevent future opioid use and to address harms caused by the opioid epidemic; such efforts may be especially important for low-income individuals, since many areas in the U.S. have a shortage of mental health services for such persons.⁵⁶² As noted throughout this report (e.g., Section 1A and Section 2E), expanding services for pain management – including mental health counseling – is essential to reducing demand for opioids. Chronic pain and mental health disorders have a bidirectional relationship, where pain can worsen mental health, and vice-versa.⁵⁶³ A population-based study of randomly selected adults, found that study participants with neck or back pain were 2.5 times more likely to experience depression within the following 12-months.⁵⁶⁴ Conversely, participants who were pain-free and had depression at the start of the study were four-times more likely to develop pain within 12-months than were participants who did not have depression at baseline. However, there are multiple barriers, including stigma, to accessing mental health treatment. A 2018 study found that, among those who were unable to access mental health treatment, 38% reported cost and lack of affordability, 21% did not know where to go for services, and 20% did not have adequate health insurance coverage for mental health services.⁵⁶⁵
174. Bereaved parents and family members often require additional support to process and address their “disenfranchised grief.” However, when they receive proper support in the years following a death due to substance use, many family members can attain “posttraumatic growth” following the traumatic event.⁵⁶⁶ Such growth occurs when positive psychological change results from exceptionally challenging life events. Grief support is key to facilitating this growth, where bereaved family members can process the complex emotions of stigma, guilt, anger, shock, and grief among individuals with shared experiences or understanding. While support networks may not be beneficial for everyone, it is important to have facilitators or counselors that can reorient individuals who may be “stuck” replaying memories or emotions from the past and identify new possibilities in life moving forward.⁵⁶⁷
175. Cognitive Behavioral Therapy (CBT) is the most frequently used psychological intervention for adults with chronic pain. Such approaches seek to improve mental health and well-being by identifying and changing maladaptive thoughts, emotions, and behaviors. Randomized trials of CBT for pain patients indicate that CBT can produce significant improvement in chronic pain and functional limitations.⁵⁶⁸ Many patients also benefit from mindfulness-based stress reduction, and from acceptance-based therapies,⁵⁶⁹ such as Acceptance and Commitment Therapy, that combines acceptance and mindfulness to promote psychological adaptability and behavior change. Clinicians and mental health counselors who treat children can provide most effective care when they receive additional training to address developmental needs within a trauma-informed approach.⁵⁷⁰

CONFIDENTIAL

176. In conclusion, abatement efforts should provide for mental health counseling for children affected by the epidemic, grief support services for bereaved family members, and psychological intervention for individuals with chronic pain. Providing mental health counseling to individuals affected by the opioid epidemic is necessary to address both the harms caused by opioids and to prevent future opioid use from chronic pain and risk-taking or maladaptive coping behaviors among individuals including youth.

CONFIDENTIAL

CATEGORY 4: ADDRESSING NEEDS OF SPECIAL POPULATIONS

Many groups of individuals have been uniquely affected by the opioid epidemic, including: pregnant women, new mothers, and infants; children and families; adolescents and young adults; older adults; Black, Indigenous, and People of Color (BIPOC); individuals experiencing homelessness; and individuals with complex pain. While some abatement remedies, such as naloxone distribution and training, generally need not be highly customized, there are other remedies that should be carefully designed with specific populations in mind.

A. PREGNANT WOMEN, NEW MOTHERS, AND INFANTS

This abatement remedy focuses on pregnant women and new mothers who have chronic opioid dependence, non-medical opioid use or OUD, as well as infants born with neonatal opioid withdrawal syndrome (NOWS), a condition among newborns that is a consequence of in utero exposure to opioids. (NOWS is also sometimes referred to neonatal abstinence syndrome [NAS], although the latter is a less specific term that in certain contexts may refer to in utero exposure to other substances such as alcohol or tobacco.) As with other special populations, pregnant women, new mothers, and their newborns are important to consider because of the ways that abatement remedies should be designed to address their unique needs and vulnerabilities.

177. The opioid epidemic has severely impacted pregnant women, new mothers, and infants. Approximately 15% of commercially insured women and 22% of women on Medicaid filled an opioid prescription during their pregnancy between 2000 and 2011.^{571,572} Prescription opioid use remains common during pregnancy; a CDC analysis of 2019 data from the Pregnancy Risk Assessment Monitoring System (PRAMS) reported that one in fifteen (6.6%) of respondents reported prescription opioid use during pregnancy.⁵⁷³ This is important because the rate of NOWS has increased as opioid prescribing has increased. For example, in an analysis of hospital discharges from 2009 to 2012, the estimated rate of NOWS increased from 3.4 to 5.8 per 1,000 hospital births nationwide.⁵⁷⁴ A longer time horizon provides similar evidence, with estimates of the diagnosis of NOWS increasing from 1.2 to 8.0 per 1,000 live births between 2000 and 2014 nationwide; during this time period, some states experienced as large as a ten-times increase.⁵⁷⁵ An analysis of national inpatient data between 2010 and 2017, found the rate of NAS increased from 4.0 to 7.3 per 1,000 births.⁵⁷⁶ Estimated maternal opioid-related diagnoses rates also significantly increased from 3.5 to 8.2 per 1,000 hospitalizations.⁵⁷⁷

178. Both SAMHSA and the American College of Obstetricians and Gynecologists (ACOG) have provided similar recommendations for targeting and treating pregnant women and neonates impacted by the opioid epidemic, including with respect to prenatal screening for opioid use among women who are pregnant, MAT treatment for pregnant women with OUD, neonatal care for neonates born with NOWS, and residential transition programs for pregnant women and new mothers with OUD who have limited social supports.^{578,579} Though individual models may differ for the immediate and long term care of children and mothers affected by opioids, generally the most successful models incorporate: (1) dyadic or family-centered models that provide direct care for both children exposed to opioids and medical and addiction care to help parents maintain recovery; (2) comprehensive pediatrics programs with multidisciplinary and long-term care for children, linked with care for parents as needed; and (3) specific developmentally-focused pediatrics programs that provide longitudinal developmental evaluations and support.⁵⁸⁰ Researchers and health providers have

CONFIDENTIAL

emphasized the importance of maintaining family relationships (i.e., family-centered treatment), which improves health and socioemotional outcomes for women and children.^{581,582}

179. Prenatal screening. SAMHSA and ACOG strongly recommend screening pregnant women for substance use disorders including OUD. ACOG specifically recommends universal screening as part of obstetric prenatal care visits, and both suggest using validated screening tools such as the National Institute on Drug Abuse's Quick Screen or Substance Use Risk Profile–Pregnancy (SURP-P).⁵⁸³ Both organizations also suggest screening be incorporated into an algorithm such as SBIRT or STIR as discussed in Paragraph #189.⁵⁸⁴ The decision to initiate MAT upon an initial visit, as compared with referral for follow-up care, should be informed by a number of factors, including the context of the visit, stability and preferences of the patient, and availability and likelihood of suitable follow-up.
180. MAT treatment. SAMHSA and ACOG suggest pregnant women with OUD be treated with MAT. This is partly due to concerns that other treatment approaches, such as abstinence, pose an increased risk of fetal injury or demise. MAT treatment should focus on the provision of buprenorphine and methadone, rather than naltrexone, since there is less information on how naltrexone may impact fetal development. Such treatment is important in custodial as well as community settings, and fortunately, there are examples of many effective, local programs that provide MAT, medical, and behavioral health care to pregnant and postpartum women.⁵⁸⁵
181. Neonatal care. Expression of NOWS is widely variable, though long-term complications may include poor neurological and motor development.⁵⁸⁶ Infants at risk of presenting with NOWS may require specialized care such as hospitalization within a neonatal intensive care unit, although it is difficult to predict the severity of withdrawal symptoms a given newborn is likely to have.⁵⁸⁷
182. Residential transition programs. Pregnant women and new mothers also need stable environments for their own health, their babies' health, and for the best chance for positive treatment outcomes. A stable environment includes long-term housing, child-care, access to transportation, all within a family-oriented and supportive environment. Some pregnant women with OUD will require residential treatment because of limited economic capital and/or serious medical illness or behavioral health needs. When possible, it is important to include additional members of the family (e.g., partner) in treatment or residential programs, because when family members progress through treatment, the short- and long-term outcomes for children and parents improve.⁵⁸⁸
183. Psychosocial supports. The majority of pregnant women and new mothers with OUD have experienced significant traumas, such as a history of sexual assault and/or domestic violence.⁵⁸⁹ Pregnant women and new mothers must be provided with psychosocial supports to cope with past traumas, the life-changes of a newborn, and progression through recovery in order to successfully remain in recovery. Women should also be taught life-skills and provided with job skill and education courses. Wraparound services for pregnant women, new mothers, and infants such as childcare for appointments, assistance with basic needs, and case management are crucial for treatment retention and success. Family navigators may also be used to provide intensive case management to each family, through a family needs assessment, individualized plan, and providing guidance through the available services and resources.

CONFIDENTIAL

184. In conclusion, abatement programs across the U.S. should include resources for pregnant women, new mothers, and neonates impacted by the epidemic. Such resources generally should include: universal screening to identify and treat pregnant women with OUD as early as possible; longitudinal services to support women and address modifiable risk factors throughout their pregnancy; clinical and behavioral interventions in the peri- and post-partum period; hospital and child welfare resources to comply with the Child Abuse Prevention and Treatment Act to ensure a plan of safe care is implemented for the infant and family or caregiver before the infant is discharged from the hospital; and follow-up services to optimize care for the mother-child dyad following hospital discharge, including the required developmental assessment for early intervention if the child is placed in out-of-home care. All infants born exposed to opioids should receive developmental support through special education beginning immediately after birth. Pregnant women with OUD and new mothers of infants exposed to opioids should receive intensive biopsychosocial services and, if needed, housing. When possible, the entire family should receive treatment and family-strengthening interventions in order to promote long-term socioemotional health.

CONFIDENTIAL

B. ADOLESCENTS AND YOUNG ADULTS

The goal of this remedy is to address the direct impact of opioid use, addiction, and overdose on children, adolescents, and young adults, including prevention programs that delay initiation or escalation of opioid use as well as screening and treatment programs that are customized to the unique needs of these special populations.

185. Children and adolescents are uniquely vulnerable to the consequences of non-medical opioid use, and as the opioid epidemic has flourished, many children and adolescents have been exposed. In 2019, 567,000 (2.3%) of adolescents aged 12 to 17 years reported past year non-medical prescription opioid use.⁵⁹⁰
186. The American Society of Addiction Medicine recognizes adolescents (aged 11-21 years), as a special population of interest with respect to substance use disorders.⁵⁹¹ Not only has early initiation of drug use been strongly associated with a constellation of adverse consequences, such as poor peer and familial relationships, and entanglements with the juvenile justice system,⁵⁹² but the ongoing brain development in adolescents during this period of time makes them highly vulnerable to substance use disorders.⁵⁹³ Because of their vulnerability and future potential, prevention and early detection of substance use disorders in youths should be heavily prioritized to minimize the short- and long-term consequences associated with drug use at an early age.
187. Several school-based or family-based prevention programs have successfully delayed or prevented initiation or escalation of drug use in youths.^{594,595,596} For example, the Life Skills Training (LST), a widely used school-based module, has been demonstrated in several controlled studies to reduce substance use amongst adolescents,⁵⁹⁷ including the reduction of non-medical prescription opioid use.⁵⁹⁸ The impact of LST may be enhanced when coupled with the Strengthening Families Program (SFP), a family-based intervention designed to develop and support family bonds and communication. Greater investment should be made in the continued dissemination, implementation, and evaluation of these and other evidence-based programs that are focused on primary prevention through education of broad populations regarding the nature of OUD, risks of non-medical opioid use, and availability of treatment and recovery support.
188. Treatment for adolescents with substance use disorder requires a unique approach and should be delivered by individuals with specialized training in the care of this population. For example, unlike older adults who have often spent years coping with substance use accompanied by a deterioration in psychosocial domains such as loss of job or family, adolescent users tend to present at treatment after only a few years of addiction. In contrast to adults with substance use disorders, adolescents' drug use is often driven by different factors (e.g., familial discord), may be subject to different environmental influences (e.g., peer effects), and may compromise psychological and social development.⁵⁹⁹
189. A subset of adolescents participating in prevention programs will be identified as high risk. These individuals should be further evaluated through formal screening such as Screening, Treatment Initiation and Referral (STIR).⁶⁰⁰ In two randomized trials focused on tobacco dependence⁶⁰¹ and OUD,⁶⁰² respectively, STIR has been demonstrated to achieve better outcomes than another screening tool, Screening, Brief Intervention, and Referral to Treatment (SBIRT), developed primarily for alcohol use disorder. STIR is not predicated upon the availability of follow-up treatment or an

CONFIDENTIAL

individual's motivation to seek it and takes into account the fact that there are FDA-approved pharmacotherapies for OUD.

190. Use of MAT is recommended for adolescents with severe opioid use disorders. Buprenorphine and naltrexone may provide more suitable treatments for adolescents than methadone, since these can be administered in office-based treatment settings. Furthermore, one of several evidence-based psychosocial therapies should be used simultaneously with MAT when treating adolescents with substance use disorders. One type of psychosocial therapy is family-based therapy, which aims to reduce the adolescent's drug use by involving the youth's family members in the treatment process. This mode of therapy facilitates the development of emotional support and communication strategies in order to address issues such as antisocial behavior or dysfunctional family interactions.
191. In conclusion, abatement programs should include resources to reach at-risk children and adolescents through school and community-based youth programs. In addition to screening and primary prevention programs to teach and reinforce positive life skills, resources should also be committed to the care of children and adolescents with non-medical opioid use or OUD, which may require expansion of personnel with customized expertise in this area, as well as resources to support the expansion of both pharmacologic and non-pharmacologic treatment and recovery services.

CONFIDENTIAL

C. FAMILIES AND CHILDREN

The goal of this remedy is to improve the resources available to support children who have been orphaned by the epidemic, as well as to assist children and their families who have otherwise been impacted and who may be served through child protective services.

192. The opioid epidemic has severely impacted many families and, at times, forced children to be separated from parents and placed in foster care. Much of the increase in the foster care population between 2012 and 2017 is attributable to the opioid epidemic.^{603,604} During the 2020 fiscal year, 631,832 children were served by the foster care system.⁶⁰⁵ Of the 217,000 children that entered foster care in 2020, over 75,000 (35%) were placed in out-of-home care for whom parental substance use was reported as a factor in the reason for removal.⁶⁰⁶ However, states vary in reporting on this variable and these data are considered an undercount of the prevalence of substance use among child welfare cases nationwide.^{607,608,609} Vastly more children – as many as one in eight – live in a household with one or more parents who have a history of past year substance use disorder.⁶¹⁰ An estimated 623,000 parents with OUD reside with a child under 18 years of age.⁶¹¹ One ecological study between 2001 and 2011, found that hospital discharges for prescription opioid overdoses were positively associated with increases in hospital discharges for child maltreatment and injury, after controlling for other substance use and environmental factors.⁶¹²

193. While the precise number of foster care placements that are directly due to opioids is unknown, a mixed-methods study commissioned by the U.S. Department of Health and Human Services provides additional context.⁶¹³ Geographic regions of the country with higher rates of overdose deaths and drug-related hospitalizations also have higher child welfare caseloads, as well as more severe and complex child welfare cases. In addition, many key informants reported worsening conditions, such as overdose deaths and caseload numbers, between 2015 to 2017. The report also identified many barriers to treatment of impacted families, including misunderstanding and mistrust of MAT, piecemeal substance use assessments, shortages of family-friendly treatment, and an increasing shortage of foster care homes. The report concluded that while these findings may not represent every geographic region or state, they nevertheless suggest how the opioid crisis has taken an unusual toll on an already strained child welfare system.

194. Children entering the foster care system, including those whose entry has been driven by the opioid epidemic, have both medical and non-medical needs. Federal and state governments often provide support to guardians of foster children for non-medical needs such as food, clothing, and housing. Many children in foster care also have special health care needs, given the high prevalence of chronic medical, developmental, and mental health problems, most of which predate placement in foster care.⁶¹⁴ Lastly, approximately 21-23% of children exiting foster care are adopted.⁶¹⁵ Though some adoption costs are offset with government subsidies, the adoption process can nevertheless impose a heavy economic burden on some families.

195. Child protective services (CPS) includes a variety of interventions that are undertaken by state agencies charged with optimizing the health and welfare of otherwise vulnerable infants, children, and adolescents. Such services include the investigation of reports of child abuse or neglect as well as the delivery of services, such as specialized case management and multisystemic or other family-based therapy, to support children and families where abuse or neglect has taken place or is likely. One such approach is Parent-Child Interaction Therapy (PCIT), an evidence-based and family-

CONFIDENTIAL

centered treatment approach that supports the development of parenting skills, while reducing negative parent-child interactions. There is a broad evidence-base supporting the value of PCIT in achieving a host of positive outcomes, including decreased parental stress and use of corporal punishment and increased parent-child interactions.⁶¹⁶ Both PCIT and, more broadly, CPS are based on several underlying principles including a recognition that a safe and permanent home is the best location for children to be raised and that most parents want to be good parents to their children.⁶¹⁷

196. In conclusion, abatement programs across the U.S. should prioritize permanency and include resources to support the needs of children who have been orphaned by the epidemic or who have lost a parent, whether or not they have entered the foster care system. In addition, abatement remedies should include resources, including intensive case management and access to therapy, to support the needs of children and adolescents who may have entered child protective services or otherwise come to the attention of social services organizations due to the opioid epidemic.

CONFIDENTIAL

D. OLDER ADULTS

The goal of this remedy is to reduce harms accruing from the opioid epidemic among older adults. This is important in part because older adults have a high prevalence of chronic pain. In addition, they may be more susceptible to adverse effects from opioids, both because of changes in drug metabolism that occur with age as well as their frequent use of concomitant medicines that may cause potentially serious drug-drug interactions.

197. Older adults represent an often-overlooked subpopulation that has been uniquely affected by the opioid epidemic. However, chronic pain is common among these individuals. For example, an analysis of the 2016 National Health Interview Survey (NHIS) found that one in four (27.6%) adults aged 65 to 84 and one in three (33.6%) adults aged 85 and older had chronic pain;⁶¹⁸ 10.7% of adults aged 65 to 84 and 15.8% of adults aged 85 and older had high-impact chronic pain. Findings from the 2019 NHIS show that the prevalence of chronic pain among older adults has remained high, with nearly one in three (30.8%) adults aged 65 and older reporting chronic pain and 11.8% reporting high-impact chronic pain.⁶¹⁹
198. Given the high prevalence of chronic pain, it should come as no surprise that opioid utilization is common among this population. For example, in 2016, one-third (33%) of Medicare Part D beneficiaries received a prescription opioid; this proportion decreased to 29% in 2018, while the number receiving MAT and naloxone prescriptions increased.^{620,621} More recently, an analysis of the 2018-2019 Medical Expenditure Panel Survey Household Component, a national survey of Medicare beneficiaries aged 65 years and older, found that one in seven (15.8%) filled at least one opioid prescription, and nearly one in twenty (4.9%) obtained five or more opioid prescription fills or refills within the previous three to six months.⁶²²
199. While high rates of opioid utilization among the elderly are concerning even when taken in isolation, many older adults also take other prescription or over the counter drugs that may pose unacceptably high risks of polypharmacy^{bb} or drug-drug interactions.⁶²³ For example, as I discuss in **Appendix E**, concurrent dispensing of benzodiazepines or other sedatives and opioids increases the risk of overdose and death.^{624,625} Beyond overdose, the concurrent use of prescription opioids and other common medications is associated with an elevated risk of falls and fractures.^{626,627}
200. In addition to high rates of opioid use, there has been a notable increase in opioid-related morbidity and mortality among adults aged 55 years and older.⁶²⁸ Between 1999 and 2019, the opioid overdose mortality rate among persons aged 55 years or older rose 1,189%, from 0.9 per 100,000 to 10.7 per 100,000.⁶²⁹ In 2018, individuals aged 75 years and older had the highest prevalence of opioid-related inpatient hospitalizations relative to other adults.⁶³⁰ Despite the increasing rate of opioid-related morbidity and mortality, naloxone and treatment for OUD is underutilized in this population. A 2020 report by the Office of Inspector General found that only one in four Medicare Part D beneficiaries at serious risk of misuse or overdose received a naloxone prescription.⁶³¹ In 2020, 225,546 (0.5%) of the 50 million beneficiaries enrolled in Medicare Part D received MAT.⁶³² However, there remains a large proportion of Medicare beneficiaries who may still benefit from MAT; approximately one

^{bb} Polypharmacy is often defined as the simultaneous use of five or more medications. (National Institute on Aging. The Dangers of Polypharmacy and the Case for Deprescribing in Older Adults. Published 2021. Available at: <https://www.nia.nih.gov/news/dangers-polypharmacy-and-case-deprescribing-older-adults>. Accessed July 31, 2022.)

CONFIDENTIAL

million Medicare beneficiaries received a diagnosis of “opioid abuse” or “opioid dependence”, but fewer than one in five (16%) of these individuals received MAT.⁶³³

201. In conclusion, abatement programs should include interventions that are customized to address the needs of older adults, informed by the unique ways that they have been affected by the opioid epidemic. By providing comprehensive outreach, education, and health interventions, we can reduce the impact of the opioid epidemic on older adults. Resources should focus on increasing the quality and equity of care that older adults receive.

CONFIDENTIAL

E. BLACK, INDIGENOUS, AND PEOPLE OF COLOR (BIPOC)

This abatement category focuses on the unique needs of Black, Indigenous, and People of Color (BIPOC) populations. This remedy is important because the opioid epidemic is typically portrayed as impacting young and middle-aged, working class, suburban and rural whites. However, communities and populations of color have not only been historically disenfranchised but, in some areas, have been disproportionately impacted by the opioid crisis.

202. There is a long history of race intersecting with the issue of substance use disorder in America. As the historian David Courtwright has noted, “what we think about addiction [in America] depends very much on who is addicted”.⁶³⁴ In 2017, non-Hispanic Black individuals were the third highest in opioid deaths due to any opioids (after non-Hispanic white, 19.4 deaths per 100,000 people, and American Indian/Alaska Native (AIAN), 15.7 deaths per 100,000 people); they were the second highest due to synthetic opioids after non-Hispanic whites (11.9 deaths per 100,000 people).⁶³⁵

203. Opioid overdose mortality among AIAN populations has steadily risen over the last two decades. The national rate of fatal opioid overdose in AIAN populations rose from 2.9 deaths per 100,000 in 1999 to 14.2 deaths per 100,000 in 2018, representing nearly a 500% increase in opioid-related mortality in the course of almost two decades.^{636,637} At a national level, AIAN populations have one of the highest rates of opioid-related mortality;⁶³⁸ at local levels, such as in Washington, AIAN mortality is at least two-times higher than non-Hispanic whites.⁶³⁹ AIAN’s also have the highest incidence of opioid misuse based on the 2020 National Survey on Drug Use and Health, with past year misuse of opioids occurring in 6.4% of AIAN individuals compared to 3.4% in non-Hispanic whites and 3.7% in Black populations.⁶⁴⁰

204. From 2019 to 2020, Black and AIAN populations experienced disproportionate increases in overdose mortality, with substantial variation by age, gender, and socioeconomic factors.⁶⁴¹ In these two years, the overdose death rate increased 44% for Black persons, 39% for AIAN, 22% for white persons, and 21% for Hispanics. However, Black persons aged 15 to 24 years and AIAN females aged 25 to 44 years experienced the largest relative increase in overdose deaths (86% and 88%, respectively). A separate analysis found that, among individuals aged 55 years and older, Black males represented a disproportionately high number of opioid overdose deaths since 2013.⁶⁴² In 2020 alone, Black males aged 65 years and older had a six-times higher overdose death rate compared to white males.⁶⁴³ Among decedents, the prevalence of ever receiving treatment for substance use disorder among people of color was substantially less than that of white decedents (Black, 8.3%; AIAN, 10.7%; Hispanic, 10.2%; white, 16.4%). In 2020, overdose death rates among Black and AIAN individuals were highest in counties with substance use treatment capacity, including MAT providers, highlighting continued inequity in access to care for BIPOC populations.

205. Systemic barriers continue to contribute to the high rate of injuries and deaths from opioids among people of color. These range from housing to education to health care access, which are important to consider when designing and evaluating interventions focused on prevention, treatment, and recovery.^{644,645} There are many pathways where racial/ethnic bias may affect the quality of health care that they receive. Studies have found that treatments that patients ultimately receive are impacted by race and ethnicity; ranging from stereotypes regarding pain thresholds of people of color and their counterparts to different expectations regarding whether and how quickly pain resolution should be achieved.^{646,647}

CONFIDENTIAL

206. SAMHSA's Tribal Technical Advisory Committee notes that determining universal rates and risks of substances misuse is challenging due to the diversity and geographical dispersion of AIAN populations, resulting in varied estimates across different regions and tribes. For example, for the states of Idaho, Oregon, and Washington, the Northwest Portland Area Indian Health Board reported that from 2006 to 2012, of drug overdose deaths, 65.3% of AIAN deaths were from prescription drugs, and of those, 77.2% were from opioids.⁶⁴⁸ AIAN adolescents have also been affected quite heavily, with estimated 2012 rates of non-medical use of prescription opioids twice as high as that of non-Hispanic whites and three times as high as that of Black adolescents.⁶⁴⁹ Furthermore, though nearly three in four AIAN individuals live in rural, urban, and suburban areas,⁶⁵⁰ only ~2% of Indian Health Service (IHS) funding is used to support urban Indian health clinics.⁶⁵¹ AIAN populations are also more vulnerable to risk factors that increase the risk of both OUD as well as mortality, such as poverty, unemployment, and alcoholism.⁶⁵²
207. Treatment and wrap-around services for non-English speakers are also important for treatment enrollment and retention. A study published in 2022 using 2019 NSDUH data investigated the utilization and need for OUD treatment by sociodemographic characteristics.⁶⁵³ This study found that MAT access appears to be racially patterned, where non-Hispanic whites are two-times more likely than Hispanic individuals with OUD treatment need to receive MAT. Only 15% of Hispanic individuals and 20% of Black individuals with OUD treatment need were able to access MAT. A separate study also found disparities in MAT for OUD treatment by race, where Hispanic and Black women were consistently less likely to receive MAT than non-Hispanic white women.⁶⁵⁴
208. There are challenges to successful prevention, treatment, and recovery for people of color who have OUD. For example, intergenerational substance use and polysubstance use are common among some impoverished communities impacted by historic marginalization, disenfranchisement, and discriminatory social policies and, for many, using and/or selling drugs is a means of survival.⁶⁵⁵ Black Americans may also have a fear of legal consequences should they be interested in seeking treatment. Importantly, Black populations may face more significant barriers to accessing treatment due to the influence of race, income, geography and insurance status on the ability to access treatment.
209. The opioid epidemic has also affected tribal communities in unique ways. For example, such communities face persistent funding challenges, and community members are inhibited from seeking services due to geographic distances and staffing concerns.⁶⁵⁶ Further, Western treatment programs, including MAT, may be incongruent with traditional healing practices, beliefs and ideas,^{657,658} and specialty services and types of medical care that are not available at a given facility are often purchased from the private sector through a contract health service (CHS) program, which applies a stringent eligibility criteria to determine which patients qualify for CHS funding.⁶⁵⁹
210. Because of their historic marginalization, the impact of the opioid epidemic BIPOC should be explicitly considered while designing interventions focused to support prevention, treatment, and recovery. For example, policies that differentiate or focus on supporting those with prescription opioid addiction while instituting punitive approaches against those who use heroin or illicit fentanyl may disenfranchise Black populations, just as different criminal penalties for crack and powdered cocaine did in the 1980s and 1990s.⁶⁶⁰ Abatement remedies should also be carefully considered to ensure that they are deployed to equally serve Black populations as their counterparts. This includes

CONFIDENTIAL

assessing whether and how, at least inadvertently, they may further marginalize or stigmatize Black individuals. For example, if white individuals with OUD are predominantly treated with buprenorphine, while Black individuals are predominantly treated with methadone, a program that expanded buprenorphine at the expense of methadone could inadvertently widen racial and ethnic disparities in MAT uptake.

211. For Indigenous communities, the IHS has worked to increase provider education, and access to naloxone and MAT through the Resource and Patient Management System Report and Information Processor (RRIP) program.^{661,662} From 2014 to 2019, the NIH has also funded four opioid-focused projects directed towards AIAN communities, two of which focus on researching culturally tailored interventions for AIAN communities.⁶⁶³ In addition, the NIH has published a document providing critical considerations for reviewers of research applications focused on AIAN populations.⁶⁶⁴ The National Indian Health Board provides a Tribal Opioid Response Resource Toolkit, which includes a variety of materials, tools, resources, and links to help Tribes combat the epidemic within their communities.⁶⁶⁵ Also, the National Congress of American Indians (NCAI) Opioid Initiative provides resources on responding to the opioid epidemic in tribal communities, including policy briefs and reports, webinars/trainings, and meetings/hearings.⁶⁶⁶ Additionally, Indian Country teleECHO clinic is available to support and educate providers with the goal of providing the health care needed for AIANs in their communities.⁶⁶⁷ However, in many AIAN communities, greater resources to support a more comprehensive and sustained abatement program are urgently needed.⁶⁶⁸
212. In conclusion, the opioid epidemic has severely and disproportionately impacted BIPOC communities across the U.S. Abatement efforts for BIPOC must be culturally responsive, trauma-informed, and take into consideration factors unique to each community. Support must be given to these communities to implement programs that honor and acknowledge their individual history, culture, and systemic challenges that they face.

CONFIDENTIAL

F. INDIVIDUALS EXPERIENCING HOMELESSNESS AND HOUSING INSECURITY

The goal of this abatement remedy is to focus on individuals with OUD who may be experiencing homelessness or housing insecurity. In order to be successful, abatement programs must be deployed to address the unique and pressing clinical and public health needs of these often-marginalized populations.

213. As of January 2020, Point-in-Time (PIT) estimates found that 580,466 individuals in the U.S. were experiencing homelessness, reflecting an increase in the population experiencing homelessness for the fourth consecutive year.⁶⁶⁹ However, for every individual that is homeless, many more experience “housing insecurity”, or problems with the affordability, safety, quality, or long-term stability of their housing.^{670,671}
214. Homelessness and housing insecurity are traumatic experiences that threaten individuals’ economic, psychological, social, and spiritual wellness. Once an individual is homeless, it is difficult to re-enter the workforce and attain stable housing. Many individuals experiencing homelessness also have acute and chronic physical health conditions and mental illness that require specialized treatment. However, financial and other barriers often make it impossible to receive such care, posing stressors that increase the risk of substance use disorders. For example, one national study found that among those who were experiencing homelessness and reported substance abuse in the previous year, 75% also had a mental illness.⁶⁷²
215. Substance use disorder is among the leading causes of homelessness in the country.⁶⁷³ A survey of individuals experiencing homelessness in San Francisco found that nearly one-in-three reported non-medical opioid use in their lifetime.⁶⁷⁴ Individuals who have OUD and are experiencing homelessness are also more likely to become chronically homeless and have a higher risk of overdose and mortality.⁶⁷⁵ A Boston study found opioid overdoses to be the leading cause of death among individuals experiencing homelessness; compared to those that were stably housed, individuals experiencing homelessness were nine-times more likely to die of overdose.⁶⁷⁶ Nationally, opioids are involved in 61% of overdose deaths among those that are stably housed, however, opioids are involved in 81% of overdose deaths among those that are homeless.⁶⁷⁷
216. Homelessness also drives treatment disparities in the opioid epidemic. A national study found that among all adults with OUD entering specialty treatment from 2013 to 2017, 12.5% reported experiencing homelessness.⁶⁷⁸ Compared to individuals not experiencing homelessness, people experiencing homelessness were less likely to enter outpatient treatment or receive MAT.⁶⁷⁹ Though receipt of MAT increased over time (13.7% to 25.2%) among individuals experiencing homelessness, this lagged behind increases in MAT use amongst individuals not experiencing homelessness.⁶⁸⁰
217. Prescription drug and non-medical opioid use are particularly high among youth experiencing homelessness. A survey of 451 youth experiencing homelessness in Los Angeles found that half reported prescription drug misuse in their lifetime.⁶⁸¹ Of those that misused prescriptions in the past month, one-in-four used prescription opioids alone and one-in-three used heroin. This was associated with an increased risk of future substance use, poor self-reported health, and risky sexual behaviors. The survey also found a higher risk of post-traumatic stress disorder (PTSD), depression, and suicidal ideation among youth experiencing homelessness that misused prescription drugs.

CONFIDENTIAL

218. The causes and effects of homelessness are complex and require multilayered interventions that focus on social support, trauma-informed approaches, and self-agency.⁶⁸² Individuals with OUD who are experiencing homelessness are often ineligible for many housing programs due to their substance use. However, housing and support are critical to providing an environment where individuals can focus on recovery. A study of veterans experiencing homelessness, many with OUD, reported that social support was crucial to maintaining housing and recovery.⁶⁸³ Given the high prevalence of trauma among individuals with OUD experiencing homelessness, using a trauma-informed approach and building trust are key to engaging them in care.⁶⁸⁴
219. Treatment and housing programs vary in services offered, sobriety requirements (e.g., low-barrier), and integration with the community (e.g., light-touch). Low-barrier models have been gaining support for their effectiveness in retaining clients in care since they do not require sobriety, and in doing so, account for the fact that relapse is common among individuals with OUD, including those experiencing homelessness.⁶⁸⁵ Because individuals are not penalized for relapsing, trust and rapport are built, which opens the door for engaging them in treatment. A low-barrier program in New York found that clients were more likely to continue their MAT as prescribed for OUD three-years after initiating the program.⁶⁸⁶ The Homeless Multidisciplinary Street Team, a mobile outreach program in California, included a team of specialists that sought out the highest-cost members of the homeless community (e.g., those who are repeatedly hospitalized or incarcerated) to assist them in receiving housing and other treatment in 2016.⁶⁸⁷ This program resulted in savings between \$103,000 to \$259,000 total for the city of Santa Monica by decreasing the health and public service utilization among high-cost individuals who experience homelessness. Additionally, “permanent supportive housing”, or housing with support, is another intervention that addresses chronic homelessness by integrating housing with health care, intensive case management, legal services, social service advocates, and occupational therapy. The U.S. Department of Housing and Urban Development estimates that investments in permanent supportive housing have reduced chronic homelessness by 20% between 2007 and 2019.⁶⁸⁸
220. Recovery housing is also an important component of care for some people with OUD. The National Alliance for Recovery Residences (NARR) defines four levels of recovery housing ranging from self-funded, peer-run, residential facilities where individuals can stay indefinitely (Level 1) to residential facilities that also serve as clinical treatment centers (Level 4).⁶⁸⁹ As explained by one public health officer: “Who we spend our time with, where we go, and the things we surround ourselves with all impact who we are and the decisions that we make. Many times, people in early recovery have to give up everything they’ve known... because those people, places, and things put them at risk for relapse or continued use. Early recovery can be painful and isolating. Recovery housing can fill that void with a safe place, compassionate people, and a life full of purpose and fun that doesn’t involve alcohol or drugs.”⁶⁹⁰
221. As with peer recovery coaches, evidence examining the effect of recovery housing on outcomes such as drug and alcohol use, employment and psychiatric symptoms, while limited, suggests beneficial effects.⁶⁹¹ However, concerns have also been raised regarding substandard or outright fraudulent services being provided by some recovery houses. A March 2018 report from the U.S. Government Accountability Office (GAO) examining this matter in five states underscores both the potential promise of recovery housing as well as the importance of adequate state regulatory oversight of their practices to ensure the prevention of exploitative or outright fraudulent housing practices.⁶⁹²

CONFIDENTIAL

222. In conclusion, abatement programs should include resources to reach individuals who have OUD who are also experiencing homelessness or are housing insecure. Evidence-based programs, such as Permanent Supportive Housing that provides wraparound services, should be implemented for individuals with OUD who are experiencing homelessness. By providing social support and focusing on the physical and mental health of these individuals, we can reduce the economic and public health impact of the opioid epidemic. Resources should focus on increasing treatment services, personnel, and housing for those that are homeless or housing insecure.

CONFIDENTIAL

G. INDIVIDUALS WITH COMPLEX PAIN

This abatement remedy focuses on non-opioid options for pain management and treatment. This is important because as many as two-thirds of adults with opioid misuse report pain as the reason for such misuse,⁶⁹³ and many individuals with diagnosed OUD also report chronic pain.^{694,695} Individuals that suffer from chronic pain are more likely to receive opioids, which not only increases the prevalence of prescription opioids in the community, but also increases the risk of potential opioid overdose. It is important to provide non-opioid pain management in the abatement framework in order to reduce the reliance on opioids as non-cancer pain treatment and to prevent opioid-related morbidity and mortality.

223. It is estimated that 50 million, or nearly one in five (20.4%), adults in the U.S. suffer from chronic pain (i.e., pain that lasts three or more months) and nearly 20 million, or 8% of the adult population, experience chronic pain that limits work and activities of daily living.⁶⁹⁶ Chronic pain is one of the most common reasons adults seek medical care and has been linked to opioid dependence, increasing the risk of opioid-related morbidity. Chronic pain may be complex and influenced by multiple factors ranging from biopsychosocial to environmental factors, thus requiring greater levels of supervision and care coordination.⁶⁹⁷

224. Non-opioid pharmacologic treatments for chronic pain have become increasingly common over the past decade. There are varying degrees of improvement in reported quality of life and pain scores across common conditions (e.g., osteoarthritis, fibromyalgia) for any given medication.⁶⁹⁸ For example, antidepressants, such as serotonin norepinephrine reuptake inhibitors (SNRIs), have been shown to improve pain for individuals suffering from low back pain, fibromyalgia, and diabetic peripheral neuropathy/post-herpetic neuralgia. Nonsteroidal anti-inflammatory drugs (NSAIDs) have also displayed effectiveness for osteoarthritis and inflammatory arthritis. Memantine, a cognition agent, has also been shown effective for fibromyalgia. Anticonvulsants (e.g., pregabalin, gabapentin, and oxcarbazepine) have been associated with short term improvements in neuropathic pain and fibromyalgia, however, these medications should be prescribed with caution given their potential for non-medical use and diversion.

225. Non-pharmacologic interventions for pain treatment include: psychological/behavioral therapy; exercise/movement therapies; manual therapies; and multimodal pain treatment that encompasses physical, behavioral, and integrated medical approaches that share the goal of relieving pain.⁶⁹⁹ Psychological treatments shown to be effective at reducing pain include: cognitive behavioral therapy; acceptance and commitment therapy; and mindfulness-based stress reduction.⁷⁰⁰ Exercise has been shown to improve chronic low back pain, chronic neck pain, knee osteoarthritis, hip osteoarthritis, and fibromyalgia.⁷⁰¹ One systematic literature review of non-pharmacologic interventions among community dwelling older adults found that, on a scale from zero (no pain) to ten (worst pain), pain intensity improved by 10% to 30%.⁷⁰² Interventions in this review included guided imagery, qigong, periosteal stimulation, and Tai Chi. Evidence regarding other treatments, such as acupuncture, is more variable and contested.⁷⁰³ Another systematic literature review and meta-analysis found that group-based therapy resulted in the strongest improvements in pain, catastrophizing beliefs, and pain self-efficacy for older adults.⁷⁰⁴

226. Ultimately, research has shown that self-efficacy and patient engagement are also important factors in treating chronic pain,⁷⁰⁵ highlighting the need for coordinated, multifaceted care. Such care can be promoted by social workers and case management support as well as pain specialists (Section 2E),

CONFIDENTIAL

and may be especially important for individuals with OUD and co-occurring pain. One study of 60 adults undergoing treatment for OUD with persistent pain found that engagement in an online pain self-management program significantly improved pain severity, opioid misuse measures and depressive symptoms while also improving pain self-efficacy.⁷⁰⁶

227. In conclusion, abatement programs across local communities should include non-opioid treatment options for pain management. Individuals who experience complex pain are at an increased risk of developing OUD or other opioid-related morbidity and mortality. As such, they should receive non-opioid pharmacologic, non-pharmacologic, or a combination of the two, as appropriate. This promotes the public health of individuals living in the U.S. by reducing the prevalence of opioids in the community and the likelihood that individuals will develop OUD as a result of opioid treatment for chronic pain.

CONFIDENTIAL

VI. MEASURING THE SUCCESS OF ABATEMENT EFFORTS

228. Communities across the U.S. are already undertaking many evidence-based abatement interventions that reflect the overarching principles, as well as strategies, that I outline above. For example, many have active, although resource constrained, drug courts; there has been a concerted effort to distribute naloxone and train individuals in its use through the community-based programs; and several programs address complications from the epidemic (e.g., SSPs), including for rural populations (e.g., mobile treatment units). Key partners include, but are not limited to, the recovery community, local public health agencies, community coalitions, harm reduction organizations, treatment providers, and first responders.
229. Data – and measurement – is vital to these efforts, a fact that is affirmed by many stakeholders, including the Centers for Medicare and Medicaid Services, which includes “Data” as one of the key areas of focus to address the crisis.^{707,708} Without such information, many may be “flying blind”, no better off than an airplane pilot without access to the plane’s instrument panel. Section 1G outlines in detail the evidence base supporting surveillance and the uses of such data.
230. The core measures in a community’s ultimate abatement plan should represent essential outcomes selected because of their linkage to abatement goals and their ability to capture key consequences of improved prevention, treatment, and recovery services. Each measure should be assessed on a quarterly, biannual, or annual basis, understanding that the more frequent an assessment occurs, the more rapidly such information can be used to iteratively inform further abatement. Such measures should provide a means of performing high-level evaluation of the global effects of abatement efforts on central outcomes of vital clinical and public health importance. Examples of potential measures include:
- Rates of fatal and non-fatal opioid overdose in the general community and in special populations (e.g., BIPOC populations)
 - Heroin/illicit fentanyl overdose death rate
 - ED visits or hospitalizations related to opioids
 - Naloxone administrations and reversals in the community
 - Rate of infants born with neonatal abstinence syndrome
 - Rate of complications associated with opioid use
 - Rate of individuals newly experiencing homelessness or housing insecurity
 - Duration of homelessness
 - Perceived benefit of and access to culturally appropriate and trauma-informed care among BIPOC^{cc}

During the coming years, as additional resources are invested in reducing the oversupply of opioids and attendant harms, there will also be opportunities to continue to enhance, collate, link, and centralize measures with others that capture other dimensions of the epidemic, including: the accessibility and quality of both pain and OUD treatment; treatment delivery within the criminal justice system; and the performance of the care delivery system for other populations, such as the commercially insured, for which the state or county may not serve as payer.

^{cc} Evaluation methods should include both qualitative and quantitative (e.g., number of patients inducted in treatment, duration of treatment) measures

CONFIDENTIAL

VII. ESTIMATED IMPACT OF PROPOSED ABATEMENT REMEDIES

231. There is intuitive scientific appeal in using randomized experiments to assess the effectiveness, and comparative effectiveness, of different interventions to reduce opioid-related morbidity and mortality. However, such investigations are impractical, and often unethical as well.⁷⁰⁹ As a result, policymakers and other stakeholders must rely upon observational evidence that is prone to shortcomings. For example, the effect of an intervention such as a naloxone law may be delayed, obfuscated by other contemporaneous policy changes, or associated with unintended effects that diminish its ultimate welfare impact. Indeed, many studies examining the impact of various abatement remedies have assessed multiple simultaneous interventions, such as an intervention to reduce opioid oversupply that combines educational outreach to clinicians with clinical decision support instituted within electronic medical records. These challenges underscore the importance of continued study by clinicians and public health experts, as well as investments such as the National Institutes of Health's HEAL Initiative.⁷¹⁰
232. While some may argue that "further research is needed", there is already a vast scientific evidence base to support the abatement interventions discussed herein. For example, there is unequivocal evidence of the benefits of treatment for OUD, the life-saving potential of naloxone, and the value of investments made in children and families impacted by substance use disorder. While using this evidence to estimate the expected impact of specific interventions within specific communities is prone to uncertainty, some general conclusions regarding abatement impact can be drawn.
233. First, the impact of treatment for OUD on reducing OUD rates over time, which represents one of the most important, and costly, interventions prescribed in this report, has been well described. For example, in a systematic review and meta-analysis of MAT, the pooled all-cause mortality was 0.92 (95% confidence intervals [CI] 0.79-1.04) per 1,000 person-years among individuals during treatment, 1.69 (CI 1.47-1.91) among those after treatment and 4.89 (CI 3.54-6.23) among those who were untreated.⁷¹¹ In another careful and comprehensive systematic review and meta-analysis, Sordo and colleagues found that the pooled all-cause mortality rates were 11.3 and 36.1 per 1,000 person-years in and out of methadone treatment (unadjusted out-to-in rate ratio 3.20, CI 2.65-3.86), and 4.3 and 9.5 in and out of buprenorphine treatment (2.20, CI 1.34-3.61).⁷¹² In other words, treatment for OUD reduced the likelihood of death by at least *a half* in these analyses.
234. Second, different interventions will have different impacts that will vary based upon the local context and magnitude of unmet need. In addition, the time horizon to see an impact from abatement efforts varies. Some investments, such as those for naloxone or treatment expansion, may produce an immediate impact, whereas others may have medium-term (e.g., drug courts, transitional housing) or long-term (e.g., child and family services) effects that may be no less important to a community's ultimate recovery.
235. Third, the return on investments from some programs can be quite profound. In other words, improving treatment uptake and use for OUD is not just the right clinical thing to do, it also makes good economic sense, in part because OUD has so many direct and indirect costs. For example, Ettner and colleagues⁷¹³ and Gerstein and colleagues,⁷¹⁴ have estimated at least a 7:1 return on investment when examining the economic benefits and costs of the treatment of alcohol and drug disorders using

CONFIDENTIAL

California treatment data.^{dd} Similarly, an analysis of a naloxone distribution program in North Carolina, as described in Section 2F, estimated that, on average, for every dollar spent on the program, there was \$2,742 of benefit due to opioid overdose deaths avoided.⁷¹⁵ In a separate decision analysis from the University of San Francisco, investigators estimated that providing naloxone to heroin users is robustly cost-effective, and possibly cost-saving, with one overdose death prevented for every 164 naloxone kits distributed.⁷¹⁶ Yet other work has examined potential savings associated with investments in harm reduction such as SSPs, suggesting that for every dollar invested in SSPs, at least six dollars are saved due to HIV prevention alone.⁷¹⁷ A separate cost-effectiveness analysis of an SSP in New York City estimated that the program would result in a baseline one year savings to the government of \$1,300 to \$3,000 per client.⁷¹⁸

236. Fourth, as noted in Paragraph #17, “the cost of doing nothing is not nothing”.⁷¹⁹ The opioid epidemic has worsened over more than two decades nationally and, for a long time, was hidden in plain sight. Fortunately, there is acknowledgement of the devastation that opioids have caused for many communities. In addition, a great deal of scientific effort has been expended to develop an evidence base regarding the approaches noted herein. This overwhelming evidence explains the strong scientific consensus regarding the importance of the abatement remedies proposed.

237. While further extrapolation is required to estimate the combined, community-level impact of interventions I propose, we^{720,721} and others^{722,723,724,725,726,727} have developed models to understand the expected degree to which different services and programs are likely to reduce opioid-related harms. If implemented in a coordinated and comprehensive fashion, the interventions I propose can reduce cumulative opioid overdoses and opioid-related harms substantially over ten to fifteen years. This estimate is based on models that have been developed, as well as review and synthesis of additional assessments of many of the interventions proposed herein, ranging from Health Professional Education (Section 1A) to Harm Reduction interventions (Section 1D), to Distributing Naloxone and Providing Training (Section 2F).

^{dd} These analyses were not limited to those with OUD. While the reports nevertheless suggest the value of OUD treatment, including MAT, there is also a need for further research focused exclusively on OUD treatments rather than broader substance use disorders.

CONFIDENTIAL

VIII. POTENTIAL OBJECTIONS TO PROPOSED ABATEMENT REMEDIES

There is remarkable consensus among public health experts regarding the abatement remedies outlined above. Nevertheless, some might object to one or more of the proposed remedies on a number of grounds.

238. Enough is already being done. One argument is that there is already an enormous amount of effort being devoted to the opioid epidemic, as well as some signs that things are “turning around”. For example, prescription opioid volume has declined overall in the U.S. since 2012 (Paragraph #22). While such arguments might have some appeal, they overlook the complexity of the epidemic, continued evidence of grave harms both nationally and locally, and the fact that investments made thus far pale in comparison to the epidemic’s societal costs. For example, despite declines in opioid sales, prescribing rates remain far above pre-epidemic baselines. Similarly, the rate of overdoses has increased substantially since 2020, and there is no indication that supply of illicit fentanyl has been stopped. As noted throughout my report, there are vast gaps that remain in the treatment system, and many of the most damaging consequences of the epidemic, such as its effects on children, families, and those with active addiction or a history of OUD, will endure for generations.

239. There may be unintended consequences. Concern has been raised regarding potential unintended consequences of efforts to address the epidemic, especially “supply-sided” interventions such as clinical guidelines that may reduce the volume of opioids used in clinical practice (Section 1A).^{728,729} It is theoretically possible that reductions in opioid prescribing may pose a burden for individuals in whom opioids are clinically appropriate, and thus, underscores the importance of multifaceted approaches to diminish this likelihood, including: investments in pain research; continued evidence generation and synthesis such as the activities undertaken by the CDC and professional societies, provider and patient education; insurance coverage and benefit redesign; and surveillance. Similarly, while arguments that constraining opioid oversupply “just pushes people to heroin” are over simplified,^{ee} such concerns underscore the urgency of expansions in the treatment system to accompany supply-sided interventions reducing the flow of people from the general population into opioid use disorder.

240. We shouldn’t reward bad behavior. Variations on this argument include that people who are “running into trouble” should know better, or more abhorrently still, “three strikes and you are out”.^{ff} These approaches to managing the opioid epidemic blame the victims and reflect classic stigmatizing language grounded in erroneous beliefs regarding the nature of addiction. No one chooses addiction any more than one chooses to have heart failure or multiple sclerosis.⁷³⁰ Such language overlooks this and conflates abuse, which is a behavior, with addiction, which is a disease. It is precisely this type of language and persistent stereotypes regarding the nature of opioid dependence, misuse, and addiction, that have slowed progress in addressing the epidemic over two decades, and that should be aggressively rebutted head-on as part of campaigns to educate the general public and health care providers regarding the nature of the epidemic. It also is hard to reconcile such views with the fact

^{ee} There is not a zero-sum game between reducing prescription opioid oversupply and increasing heroin use. For example, see Compton WM, Jones CM, Baldwin GT. Relationship Between Nonmedical Prescription-Opioid Use and Heroin Use. *New England Journal of Medicine*. 2016;374:154-63.

^{ff} Such an argument was proposed by a city council member in a small town in Ohio, who argued that the use of Emergency Medical Services should be restricted among people who utilize such services for multiple opioid overdoses.

CONFIDENTIAL

that prescription opioids used under clinical supervision still result in enormous harms⁷³¹ (see also **Appendix E**).^{732,733}

241. MAT isn't that effective and it is diverted. In fact, there is a substantial body of evidence establishing the effectiveness of treatments such as buprenorphine and methadone in retaining people in treatment, reducing illicit drug use, decreasing criminal activity and preventing overdose death.^{734,735} It is true that relapse among people with OUD is not uncommon, just as is the case with cancer, depression, and many other chronic diseases. Similarly, while treatment failures occur with MAT, the empiric response rate to many medicines, such as antidepressants, is low; this does not obviate their potential clinical and public health value. An overwhelming amount of evidence indicates that MAT can significantly decrease mortality and other undesirable outcomes, a reduction that could be seldom matched by treatments for many other chronic diseases. Nonetheless, diversion of MAT remains a concern, and underscores the importance of more, rather than less, investment in the treatment system to enhance the comprehensiveness and continuity of individuals seeking care for addiction.^{gg}
242. The problem isn't prescription opioids, it is other drugs (e.g., cocaine, alcohol, methamphetamines). The increasing presence of fentanyl within the non-opioid supply chain, as well as sharp increases in overdose deaths from stimulants such as cocaine and methamphetamine during the past few years, are the source of increasing concern on the part of clinicians, policymakers, public health officials and the general public (see Footnote c of this report). It is true that many people who overdose from opioids have other drugs in their system at the time of death, that other substance use disorders are common among those with OUD, and that there are shortcomings in our clinical and public health infrastructure to address non-opioid substance use disorders. While these sources of morbidity and mortality require a different public health response than one geared towards opioids alone, they do not diminish the importance of the efforts discussed herein addressing the historic oversupply of opioids and well delineated harms that have resulted from such.
243. The problem isn't prescription opioids, because their use has declined markedly over time. Another line of argument to support the claim that the problem isn't prescription opioids is that morbidity persists while prescribing has decreased considerably since its peak around 2010-2011. However, there is often a lag, or period of time, between an exposure to a harmful agent and associated negative health outcomes that may ensue.^{hh} For example, an individual may develop cancer after years or decades of cigarette use, and if everyone in a community stopped smoking tomorrow, rates of lung cancer would not be expected to decline for years or decades. Similarly, our work modeling the trajectory of the opioid epidemic suggests the continuing harms that may ensue years after high population exposures to opioids regardless of reductions in the number of opioid prescriptions. For example, in our model, of the 2.4 million individuals estimated to have active OUD in the U.S. in 2019, two in three (65%) initiated medical use of prescription opioids before 2011.⁷³⁶ Of the projected 38,940 fatal opioid overdoses in 2029 among people with prior prescription opioid nonmedical use, more than half (54%) initiated the medical use of prescription opioids before 2011. The median time

^{gg} The use of directly observed therapy (DOT) to deliver methadone, and provider administered buprenorphine formulations, are both additional means of reducing potential MAT diversion.

^{hh} As I note elsewhere such as Paragraph #18 and Section 4D, prescription opioids are also still oversupplied in many contexts.

CONFIDENTIAL

between prescription opioid initiation to an overdose death that occurred between 2011 and 2019 was 5.2 years.

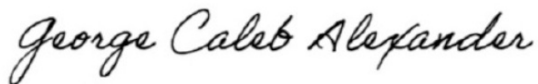
244. Cost-benefit of specific approaches is not clear. The proposed abatement plan discussed herein reflects evidence-based and evidence-informed approaches to address the epidemic. Many approaches,^{737,738,739,740} but not all,⁷⁴¹ have been subject to cost-benefit analysis in a variety of contexts. In some cases, the cost-benefit or cost-effectiveness of proposed abatement measures has been assessed specifically in the context of a single state, such as assessments of adolescent screening interventions performed by the Washington State Institute for Public Policy.⁷⁴² In other cases, comprehensive cost-effectiveness analyses that are representative of individuals with OUD in the U.S. population have been performed. For example, in an analysis that utilized Veterans Administration data and was scaled to the U.S. population, it was found that expanded access to MAT was cost-effective, yielding a savings of \$15,000 to \$90,000 lifetime costs per person with OUD, exclusive of criminal justice cost savings, due to improvements in OUD-associated morbidity and mortality.⁷⁴³ Overall, as I note elsewhere, there is a remarkable degree of consensus regarding what abatement strategies are needed, reflecting an acknowledgement of the urgency of the epidemic both nationally and locally, the large body of scientific information underpinning abatement remedies, and an awareness of the enormous costs of inaction.
245. It is unclear what success looks like. Some might argue that the success of abatement remedies is ill defined, and that without such clear benchmarks, there is no way to discern whether or not specific remedies are working, or worth it. Fortunately, there is clear consensus regarding how to abate the opioid epidemic, and this is because of the enormous body of scientific evidence underlying it. Plans must be tailored to local communities, and measurement of process and outcomes is important so as to gauge success. We are now two decades or more into the opioid epidemic, and it may take us just as long to get out of the opioid epidemic as it has to get into it. While there may be different ways of defining success (Section VII), one potential measure would be to restore pre-epidemic levels of opioid supply, rates of addiction, and overdose deaths.

CONFIDENTIAL

IX. CONCLUSIONS

246. The opioid epidemic is the worst drug epidemic in our nation's history, and it has been driven by large increases in the oversupply of prescription opioids for the treatment of pain. Communities across the U.S. have experienced first-hand morbidity and mortality attributable to the epidemic, whether with respect to rates of OUD, and non-fatal and fatal overdose, particularly in vulnerable populations such as individuals experiencing homelessness and people of color. These challenges make the substantial investments made to address the local epidemic all the more laudable. Although many measures of the epidemic, especially rates of addiction and overdose deaths, remain at alarming levels, there is increasing recognition of the magnitude of the harms that have accrued, and remarkable scientific and public health consensus regarding what needs to be done. The abatement remedies described herein represent evidence-based and evidence-informed approaches that many communities have already begun to undertake with varying degrees of coordination and scale, and which can be further applied locally, too. They are highly aligned with the three principles described at the outset of this report: (1) informing action with evidence; (2) intervening comprehensively; and (3) promoting appropriate and safe opioid use (see Section IV). As the citizens and leaders of communities across the U.S. know all too well, there is not a moment to lose.

August 22, 2022



G. Caleb Alexander, MD, MS

Baltimore, MD

CONFIDENTIAL

X. REFERENCES

- ¹ Strom BL, Kimmel SE, Hennessy S. Textbook of Pharmacoepidemiology. John Wiley & Sons. 2020.
- ² Chang HY, Daubresse M, Kruszewski SP, Alexander GC. Prevalence and Treatment of Pain in EDs in the United States, 2000 to 2010. *American Journal of Emergency Medicine*. 2014;32:421-31.
- ³ Daubresse M, Chang H-Y, Yu Y, Viswanathan S, Shah ND, Stafford RS, Kruszewski SP, Alexander GC. Ambulatory Diagnosis and Treatment of Nonmalignant Pain in the United States, 2000-2010. *Medical Care*. 2013;51:870-8.
- ⁴ Mehta HB, Kuo YF, Raji MA, Westra J, Boyd C, Alexander GC, Goodwin JS. State Variation in Chronic Opioid Use in Long-Term Care Nursing Home Residents. *Journal of the American Medical Directors Association*. 2021;22:2593-2599.e4.
- ⁵ Alexander GC, Kolodny A. Initial Opioid Prescriptions Among U.S. Patients, 2012-2017. *The New England Journal of Medicine*. 2019;380:2587.
- ⁶ Lyapustina T, Rutkow L, Chang HY, Daubresse M, Ramji AF, Faul M, Stuart EA, Alexander GC. Effect of a "Pill Mill" Law on Opioid Prescribing and Utilization: The Case of Texas. *Drug and Alcohol Dependence*. 2016;159:190-7.
- ⁷ McGinty B, Stuart EA, Alexander GC, Barry CL, Bicket MC, Rutkow L. Protocol: Mixed-Methods Study to Evaluate Implementation, Enforcement, and Outcomes of U.S. State Laws Intended to Curb High-Risk Opioid Prescribing. *Implementation Science*. 2018;13:37.
- ⁸ Rutkow L, Smith K, Lai A, Vernick J, Davis C, Alexander GC. Prescription Drug Monitoring Program Design and Function: A Qualitative Analysis. *Drug and Alcohol Dependence*. 2017;180:395-400.
- ⁹ Chang HY, Lyapustina T, Rutkow L, Daubresse M, Richey M, Faul M, Stuart EA, Alexander GC. Impact of Prescription Drug Monitoring Programs and Pill Mill Laws on High-Risk Opioid Prescribers: A Comparative Interrupted Time Series Analysis. *Drug and Alcohol Dependence*. 2016;165:1-8.
- ¹⁰ Moyo P, Griffin BA, Onukwugha E, Palumbo F, Harrington D, Alexander GC, Simoni-Wastila L. Impact of Prescription Drug Monitoring Programs (PDMPs) on Opioid Utilization Among Medicare Beneficiaries in 10 U.S. States. *Addiction*. 2017;112:1784-96.
- ¹¹ McGinty B, Stuart EA, Alexander GC, Barry CL, Bicket MC, Rutkow L. Protocol: Mixed-Methods Study to Evaluate Implementation, Enforcement, and Outcomes of U.S. State Laws Intended to Curb High-Risk Opioid Prescribing. *Implementation Science*. 2018;13:37.
- ¹² Rutkow L, Chang HY, Daubresse M, Webster D, Stuart E, Alexander GC. Effect of Florida's Prescription Drug Monitoring Program and Pill Mill Laws on Opioid Prescribing and Use. *JAMA Internal Medicine*. 2015;175:1642-9.
- ¹³ Rutkow L, Turner L, Lucas E, Hwang C, Alexander GC. Most Primary Care Physicians Are Aware of Prescription Drug Monitoring Programs, But Many Find the Data Difficult to Access. *Health Affairs*. 2015;34:484-92.
- ¹⁴ Moyo P, Griffin BA, Onukwugha E, Palumbo F, Harrington D, Alexander GC, Simoni-Wastila L. Prescription Drug Monitoring Programs: Assessing the Association Between "Best Practices" and Opioid Use by Disabled and Older Adults. *Health Services Research*. 2019;54:1045-54.
- ¹⁵ Rollman JE, Heyward J, Olson L, Lurie P, Sharfstein J, Alexander GC. Assessment of the FDA Risk Evaluation and Mitigation Strategy for Transmucosal Immediate-Release Fentanyl Products. *JAMA*. 2019;321:676-85.
- ¹⁶ Heyward J, Olson L, Sharfstein J, Stuart EA, Lurie P, Alexander GC. Evaluation of the Extended-Release/Long-Acting Opioid Prescribing Risk Evaluation and Mitigation Strategy Program by the United States Food and Drug Administration: A Review. *JAMA Internal Medicine*. 2020;180:301-9.
- ¹⁷ Heyward J, Moore TJ, Chen J, Meek K, Lurie P, Alexander GC. Key Evidence Supporting Prescription Opioids Approved by the United States Food and Drug Administration, 1997 to 2018. *Annals of Internal Medicine*. 2020;173:956-63.
- ¹⁸ McGinty EE, Bicket MC, Stuart EA, Alexander GC, Barry CL, McCourt AD, Rutkow L. Effects of State Opioid Prescribing Laws on Use of Opioid and Other Pain Treatments Among Commercially Insured U.S. Adults. *Annals of Internal Medicine*. 2022;175:617-27.

CONFIDENTIAL

-
- ¹⁹ Heyward J, Jones CM, Compton WM, Lin DH, Losby JL, Murimi IB, Baldwin GT, Ballreich JM, Thomas D, Bicket M, Porter L, Tierce JC, Alexander GC. Coverage of Nonpharmacologic Treatments for Low Back Pain Among United States Public and Private Insurers. *JAMA Network Open*. 2018;1:e183044.
- ²⁰ Lin DH, Jones CM, Compton WM, Heyward J, Losby JL, Murimi IB, Baldwin GT, Ballreich JM, Thomas D, Bicket M, Porter L, Tierce JC, Alexander GC. Prescription Drug Coverage for Treatment of Low Back Pain Among United States Medicaid, Medicare Advantage and Commercial Insurers. *JAMA Network Open*. 2018;1:e180235.
- ²¹ Daubresse M, Gleason PP, Peng Y, Shah N, Ritter ST, Alexander GC. Impact of a Drug Utilization Review Program on High-Risk Use of Prescription Controlled Substances. *Pharmacoepidemiology and Drug Safety*. 2014;23:419-27.
- ²² Saloner B, Levin J, Chang HY, Jones C, Alexander GC. Changes in Buprenorphine-Naloxone and Opioid Pain Reliever Prescriptions After the Affordable Care Act Medicaid Expansion. *JAMA Network Open*. 2018;1:e181588.
- ²³ Rao T, Kiptanui Z, Dowell P, Triebwasser C, Alexander GC, Harris I. Formulary Restrictions for Opioid Alternatives Increase Opioid Prescribing Among Medicare Beneficiaries. *JAMA Network Open*. 2020;3:e200274.
- ²⁴ Heins SE, Frey KP, Alexander GC, Castillo RC. Reducing High-Dose Opioid Prescribing: State-Level Morphine Equivalent Daily Dose Policies, 2007-2017. *Pain Med*. 2020;21:308-16.
- ²⁵ Andersen MS, Lorenz V, Pant A, Bray JW, Alexander GC. Effect of Prescription Opioid Utilization Management on Opioid Prescribing, Fatal and Non-Fatal Overdose Among U.S. Medicare Beneficiaries. *American Journal of Managed Care*. 2022;28:e63-8.
- ²⁶ Stone EM, Rutkow L, Bicket MC, Barry CL, Alexander GC, McGinty EE. Implementation and Enforcement of State Opioid Prescribing Laws. *Drug and Alcohol Dependence*. 2020;213:108107.
- ²⁷ Rutkow L, Vernick JS, Alexander GC. More States Should Regulate Pain Management Clinics to Promote Public Health. *American Journal Public Health*. 2017;107:240-3.
- ²⁸ Alexander GC, Kruszewski SP, Webster DW. Rethinking Opioid Prescribing to Protect Patient Safety and Public Health. *JAMA*. 2012;308:1865-6.
- ²⁹ Kolodny A, Courtwright DT, Hwang CS, Kreiner P, Eadie JL, Clark TW, Alexander GC. The Prescription Opioid and Heroin Crisis: A Public Health Approach to an Epidemic of Addiction. *Annual Review of Public Health*. 2015;36:559-74.
- ³⁰ Alexander GC, Stoller KB, Haffajee RL, Saloner B. An Epidemic in the Midst of a Pandemic: Opioid Use Disorder and COVID-19. *Annals of Internal Medicine*. 2020;173:57-8.
- ³¹ Nguyen TD, Gupta S, Ziedan E, Simon KI, Alexander GC, Saloner B, Stein BD. Assessment of Filled Buprenorphine Prescriptions for Opioid Use Disorder During the Coronavirus Disease 2019 Pandemic. *JAMA Internal Medicine*. 2020;181:562-4.
- ³² Ballreich J, Mansour O, Hu E, Chingcuanco F, Pollack HA, Dowdy DW, Alexander GC. Modeling Mitigation Strategies to Reduce Opioid-Related Morbidity and Mortality in the United States. *JAMA Network Open*. 2020;3:e2023677.
- ³³ Alexander GC, Mix LA, Choudhury S, Taketa R, Tomori C, Mooghali M, Fan A, Mars S, Ciccarone D, Patton M, Apollonio DE. The Opioid Industry Documents Archive: A Living Digital Repository. *American Journal of Public Health*. 2022;112:1126-1129.
- ³⁴ Guadamuz J, Alexander GC, Uddin T, Trotsky-Sirr R, Qato DM. Availability and Cost of Naloxone Spray in Philadelphia Pharmacies, 2017. *JAMA Netw Open*. 2019;2:e195388.
- ³⁵ Seamans MJ, Carey TS, Westreich DJ, Cole SR, Wheeler SB, Alexander GC, Brookhart MA. Association of Household Opioid Availability and Prescription Opioid Initiation Among Household Members. *JAMA Internal Medicine*. 2018;178:102-9.
- ³⁶ Hwang C, Chang HY, Alexander GC. Impact of Abuse-Deterrent OxyContin on Prescription Opioid Utilization. *Pharmacoepidemiology and Drug Safety*. 2015;24:197-204.

CONFIDENTIAL

-
- ³⁷ Foti K, Heyward J, Tajanlangit M, Meek K, Jones C, Kolodny A, Alexander GC. Primary Care Physicians' Preparedness to Treat Opioid Use Disorder in the United States: A Cross-Sectional Survey. *Drug and Alcohol Dependence*. 2021;225:108811.
- ³⁸ Hwang CS, Turner LW, Kruszewski SP, Kolodny A, Alexander GC. Primary Care Physicians' Knowledge and Attitudes Regarding Prescription Opioid Abuse and Diversion. *Clinical Journal of Pain*. 2016;32:279-84.
- ³⁹ Daubresse M, Saloner B, Pollack HA, Alexander GC. Non-Buprenorphine Opioid Utilization Among Patients Using Buprenorphine. *Addiction*. 2017;112:1045-53.
- ⁴⁰ Saloner B, Daubresse M, Alexander GC. Patterns of Buprenorphine-Naloxone Treatment for Opioid Use Disorder in a Multistate Population. *Medical Care*. 2017;55:669-76.
- ⁴¹ Chang HY, Daubresse M, Saloner B, Alexander GC. Chronic Disease Medication Adherence After Initiation of Buprenorphine for Opioid Use Disorder. *Medical Care*. 2019;57:667-72.
- ⁴² Anderson KE, Saloner B, Eckstein J, Chaisson CE, Scholle SH, Niles L, Dy S, Alexander GC. Quality of Buprenorphine Care for Insured Adults with Opioid Use Disorder. *Medical Care*. 2021;59:393-401.
- ⁴³ Alinsky RH, Prichett L, Chang HY, Alexander GC, Stein BD, Saloner B. Treatment of Opioid Use Disorder With Buprenorphine Among US Adolescents and Young Adults During the Early COVID-19 Pandemic. *Journal of Adolescent Health*. 2022.
- ⁴⁴ Chang HY, Kharrazi H, Bodycombe D, Weiner J, Alexander GC. Healthcare Costs and Utilization Associated with High-Risk Prescription Opioid Use: A Retrospective Cohort Study. *BMC Medicine*. 2018;16:69.
- ⁴⁵ Canan C, Polinski JM, Alexander GC, Kowal MK, Brennan TA, Shrank WH. Automatable Algorithms to Identify Nonmedical Opioid Use Using Electronic Data: A Systematic Review. *Journal of the American Medical Informatics Association*. 2017;24:1204-10.
- ⁴⁶ Chang HY, Murimi IB, Jones CM, Alexander GC. Relationship Between High-Risk Patients Receiving Prescription Opioids and High-Volume Opioid Prescribers. *Addiction*. 2018;113:677-86.
- ⁴⁷ Canan C, Chander G, Monroe A, Gebo K, Moore R, Agwu A, Alexander GC, Lau B. High-Risk Prescription Opioid Use Among People Living with HIV. *Journal of Acquired Immune Deficiency Syndromes*. 2018;78:283-290.
- ⁴⁸ Canan C, Alexander GC, Moore R, Murimi I, Chander G, Lau B. Medicaid Trends in Opioid and Non-Opioid Use by HIV Status. *Drug and Alcohol Dependence*. 2019;197:141-8.
- ⁴⁹ Canan CE, Chander G, Moore R, Alexander GC, Lau B. Estimating the Prevalence of and Characteristics Associated with Prescription Opioid Diversion Among a Clinic Population Living With HIV: Indirect and Direct Questioning Techniques. *Drug and Alcohol Dependence*. 2021;219:108398.
- ⁵⁰ Daubresse M, Alexander GC, Crews DC, Segev DL, McAdams-DeMarco MA. Trends in Opioid Prescribing Among Hemodialysis Patients, 2007-2014. *American Journal of Nephrology*. 2019;49:2031.
- ⁵¹ Novick TK, Surapaneni A, Shin JI, Ballew SH, Alexander GC, Inker LA, Chang AR, Grams ME. Prevalence of Opioid, Gabapentinoid, and NSAID Use in CKD. *Clinical Journal of American Society of Nephrology*. 2018;13:1886-8.
- ⁵² Novick TK, Surapaneni A, Shin JI, Alexander GC, Inker LA, Wright EA, Chang AR, Grams ME. Associations of Opioid Prescriptions with Death and Hospitalization Across the Spectrum of Estimated GFR. *Clinical Journal of the American Society of Nephrology*. 2019;14:1581-9.
- ⁵³ Daubresse M, Alexander GC, Crews DC, Segev DL, Lentine K, McAdams-DeMarco MA. High-Dose Opioid Utilization and Mortality Among Individuals Initiating Hemodialysis. *BMC Nephrology*. 2021;22:1-0.
- ⁵⁴ Sibia US, Mandelblatt AE, Alexander GC, King PJ, MacDonald J. Opioid Prescriptions After Total Joint Arthroplasty. *Journal of Surgical Orthopaedic Advances*. 2018;27:231-6.
- ⁵⁵ Bicket MC, White E, Pronovost PJ, Wu CL, Yaster M, Alexander GC. Opioid Oversupply After Joint and Spine Surgery: A Prospective Cohort Study. *Anesthesia and Analgesia*. 2019;128:358-64.

CONFIDENTIAL

-
- ⁵⁶ Bicket MC, Brat G, Hutfless S, Wu C, Nesbit S, Alexander GC. Optimizing Opioid Prescribing and Pain Treatment for Surgery: A Conceptual Framework. *American Journal of Health-System Pharmacy*. 2019;76:1403-12.
- ⁵⁷ Bicket MC, Murimi I, Mansour O, Wu CL, Alexander GC. Association of New Opioid Continuation with Surgical Specialty and Type in the United States. *American Journal of Surgery*. 2019;218:818-27.
- ⁵⁸ Bicket MC Long J, Pronovost PJ, Alexander GC, Wu CL. Prescription Opioid Analgesics Commonly Unused After Surgery: A Systematic Review. *JAMA Surgery*. 2017;152:1066-71.
- ⁵⁹ Jones CM, Bekheet F, Park JN, Alexander GC. The Evolving Overdose Epidemic: Synthetic Opioids and Rising Stimulant-Related Harms. *Epidemiologic Reviews*. 2020;42:154-66.
- ⁶⁰ Park JN, Rashidi E, Foti K, Zoorob M, Sherman S, Alexander GC. Fentanyl and Fentanyl Analogs in the Illicit Stimulant Supply: Results from United States Drug Seizure Data, 2011–2016. *Drug and Alcohol Dependence*. 2021;218:108416.
- ⁶¹ Lin D, Lucas E, Murimi IB, Kolodny A, Alexander GC. Financial Conflicts of Interest and Centers for Disease Control and Prevention’s 2016 Guideline for Prescribing Opioids for Chronic Pain. *JAMA Internal Medicine*. 2017;177:427-8.
- ⁶² Moynihan R, Bero L. Toward a Healthier Patient Voice: More Independence, Less Industry Funding. *JAMA Internal Medicine*. 2017;177:350-1.
- ⁶³ Anderson KE, Alexander GC, Niles L, Scholle SH, Saloner B, Dy SM. Quality of Preventive and Chronic Illness Care for Insured Adults With Opioid Use Disorder. *JAMA Network Open*. 2021;4:e214925.
- ⁶⁴ Yuanhong Lai A, Smith KC, Vernick JS, Davis CS, Caleb Alexander G, Rutkow L. Perceived Unintended Consequences of Prescription Drug Monitoring Programs. *Substance Use Misuse*. 2019;54:345-9.
- ⁶⁵ Thakrar AP, Alexander GC, Saloner B. Buprenorphine Use in Jails and Prisons in the United States, 2015-2021. *JAMA Network Open*. 2021;4:e2138807.
- ⁶⁶ Alexander GC, Ballreich J, Mansour O, Dowdy DW. Effect of Reductions in Opioid Prescribing on Opioid Use Disorder and Fatal Overdose in the United States: A Dynamic Markov Model. *Addiction*. 2022;117:969-976.
- ⁶⁷ Rollman JE, Heyward J, Olson L, Lurie P, Sharfstein J, Alexander GC. Assessment of the FDA Risk Evaluation and Mitigation Strategy for Transmucosal Immediate-Release Fentanyl Products. *JAMA*. 2019;321:676-85.
- ⁶⁸ Heyward J, Olson L, Sharfstein J, Stuart EA, Lurie P, Alexander GC. Oversight of Extended Release/Long Acting (ER/LA) Opioid Prescribing by the United States Food and Drug Administration: A Narrative Review. *JAMA Internal Medicine*. 2020;180:301-9.
- ⁶⁹ Alexander GC, Mix LA, Choudhury S, Taketa R, Tomori C, Mooghali M, Fan A, Mars S, Ciccarone D, Patton M, Apollonio DE. The Opioid Industry Documents Archive: A Living Digital Repository. *American Journal of Public Health*. 2022;112:1126-1129.
- ⁷⁰ Hill AB. The Environment and Disease: Association or Causation? *Journal of the Royal Society of Medicine*. 1965;58:295-300.
- ⁷¹ Murad MH, Asi N, Alsawas M, Alahdab F. New Evidence Pyramid. *BMJ Evidence-Based Medicine*. 2016;21:125-7.
- ⁷² Katz J. How a Police Chief, a Governor and a Sociologist Would Spend \$100 Billion to Solve the Opioid Crisis. *New York Times*. Published 2018. Available at: <https://www.nytimes.com/interactive/2018/02/14/upshot/opioid-crisis-solutions.html>. Accessed February 10, 2020.
- ⁷³ Delaney JK. *The Right Answer: How We Can Unify Our Divided Nation*. Henry Holt and Company. New York: Macmillan Publishing Group, 2018.
- ⁷⁴ Centers for Disease Control and Prevention. *Understanding the Epidemic*. Published 2018. Available at: <https://www.cdc.gov/drugoverdose/epidemic/index.html>. Accessed April 30, 2020.
- ⁷⁵ Pirani F. Opioids Now Kill More Americans than Guns or Breast Cancer, CDC Says. *Atlanta Journal-Constitution*. Published 2017. Available at: <https://www.ajc.com/news/health-med-fit-science/opioids-now-kill-more-americans-than-guns-breast-cancer-cdc-says/DUx1KS33P4sbyzgj9T9rrN>. Accessed February 10, 2020.

CONFIDENTIAL

-
- ⁷⁶ Ho Jessica Y, Hendi Arun S. Recent Trends in Life Expectancy Across High Income Countries: Retrospective Observational Study. *BMJ*. 2018;362:k2562.
- ⁷⁷ Centers for Disease Control and Prevention. U.S. Overdose Deaths in 2021 Increased Half as Much as in 2020 – But Are Still Up 15%. Updated May 11, 2022. Available at: https://www.cdc.gov/nchs/pressroom/nchs_press_releases/2022/202205.htm. Accessed May 17, 2022.
- ⁷⁸ Centers for Disease Control and Prevention. Understanding the Epidemic. Updated 2021. Available at: <https://www.cdc.gov/drugoverdose/epidemic/index.html>. Accessed June 21, 2021.
- ⁷⁹ United States Food and Drug Administration. FDA Analysis of Long-Term Trends in Prescription Opioid Analgesic Products: Quantity, Sales, and Price Trends. Published 2018. Available at: <https://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM598899.pdf>. Accessed February 10, 2020.
- ⁸⁰ Centers for Disease Control and Prevention. Vital Signs: Overdoses of Prescription Opioid Pain Relievers - United States, 1999-2008, Morbidity and Mortality Weekly Report. 2011;60:1487.
- ⁸¹ Centers for Disease Control and Prevention. U.S. Opioid Dispensing Rate Maps. Available at: <https://www.cdc.gov/drugoverdose/rxrate-maps/index.html>. Accessed July 28, 2022.
- ⁸² Centers for Disease Control and Prevention. U.S. State Opioid Dispensing Rates, 2020. Available at: <https://www.cdc.gov/drugoverdose/rxrate-maps/state2020.html>. Accessed July 29, 2022.
- ⁸³ Centers for Disease Control and Prevention. U.S. County Opioid Dispensing Rates, 2020. Available at: <https://www.cdc.gov/drugoverdose/rxrate-maps/county2020.html>. Accessed July 29, 2022.
- ⁸⁴ Centers for Disease Control and Prevention. Wide-ranging Online Data for Epidemiologic Research, Multiple Cause of Death Data. Available at: <https://wonder.cdc.gov/mcd-icd10.html>. Accessed July 29, 2022.
- ⁸⁵ Alexander GC, Stoller KB, Haffajee RL, Saloner B. An Epidemic in the Midst of a Pandemic: Opioid Use Disorder and COVID-19. *Ann Intern Med*. 2020;173:57-8.
- ⁸⁶ Volkow ND. Collision of the COVID-19 and Addiction Epidemics. *Ann Intern Med*. 2020;173:61-2.
- ⁸⁷ Nguyen T, Buxton JA. Pathways Between COVID-19 Public Health Responses and Increasing Overdose Risks: A Rapid Review and Conceptual Framework. *International Journal of Drug Policy*. 2021;93:103236.
- ⁸⁸ Becker WC, Fiellin DA. When Epidemics Collide: Coronavirus Disease 2019 (COVID-19) and the Opioid Crisis. *Ann Intern Med*. 2020;173:59-60.
- ⁸⁹ Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72,314 Cases From the Chinese Center for Disease Control and Prevention. *JAMA*. 2020;323:1239-42.
- ⁹⁰ Alexander GC, Stoller KB, Haffajee RI, Saloner B. An Epidemic in the Midst of a Pandemic: Opioid Use Disorder and COVID-19. *Annals of Internal Medicine*. 2020;173:57-8.
- ⁹¹ Christie C, Baker C, Cooper R, Kennedy PJ, Madras B, Bondi B. The President's Commission on Combating Drug Addiction and the Opioid Crisis. Published 2017. Available at: https://www.whitehouse.gov/sites/whitehouse.gov/files/images/Final_Report_Draft_11-1-2017.pdf. Accessed November 27, 2018.
- ⁹² Alexander GC, Frattaroli S, Gielen AC. The Opioid Epidemic: From Evidence to Impact. Published 2017. Available at: <https://www.jhsph.edu/events/2017/americas-opioid-epidemic/report/2017-JohnsHopkins-Opioid-digital.pdf>. Accessed February 10, 2020.
- ⁹³ National Governors Association. Governors' Recommendations for Federal Action to End the Nation's Opioid Crisis. Published 2018. Available at: <https://classic.nga.org/cms/governors-recommendations-opioid-crisis>. Accessed February 10, 2020.

CONFIDENTIAL

-
- ⁹⁴ Department of Veterans Affairs, Department of Defense. VA/DoD Clinical Practice Guideline for Opioid Therapy for Chronic Pain Version 3.0. Published 2017. Available at: <https://www.healthquality.va.gov/guidelines/Pain/cot/VADoDOTCPG022717.pdf>. Accessed February 10, 2020.
- ⁹⁵ Trust for America's Health. Pain in the Nation: The Drug, Alcohol and Suicide Crises and Need for a National Resilience Strategy. Available at: <https://www.tfah.org/report-details/pain-in-the-nation>. Accessed February 10, 2020.
- ⁹⁶ U.S. Department of Health and Human Services. Overdose Prevention Strategy. Published 2021. Available at: <https://aspe.hhs.gov/sites/default/files/documents/101936da95b69acb8446a4bad9179cc0/overdose-prevention-strategy.pdf>. Accessed June 17, 2022.
- ⁹⁷ Centers for Disease Control and Prevention. Contextual Evidence Review for the CDC Guideline for Prescribing Opioids for Chronic Pain – United States, 2016. CDC Stacks: Public Health Publications. Published 2016. Available at: <https://stacks.cdc.gov/view/cdc/38027>. Accessed March 16, 2019.
- ⁹⁸ Chou R, Deyo R, Devine B, Hansen R, Sullivan S, Jarvik JG, Blazina I, Dana T, Bougatsos C, Turner J. The Effectiveness and Risks of Long-Term Opioid Treatment of Chronic Pain. Evidence Report/Technology Assessment. 2014;218:1-219.
- ⁹⁹ National Institute on Drug Abuse (NIDA). Principles of Drug Addiction Treatment: A Research-Based Guide (Third Edition). Published 2018. Available at: <https://d14rmgtrwzf5a.cloudfront.net/sites/default/files/675-principles-of-drug-addiction-treatment-a-research-based-guide-third-edition.pdf>. Accessed February 10, 2020.
- ¹⁰⁰ Zhang Z, Friedmann PD, Gerstein DR. Does Retention Matter?. Treatment Duration and Improvement in Drug Use. Addiction. 2003;98:673-84.
- ¹⁰¹ United States Food and Drug Administration. Information About Medication Assisted Treatment. Published 2019. Available at: <https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm600092.htm>. Accessed February 10, 2020.
- ¹⁰² Centers for Disease Control and Prevention: NCHHSTP Newsroom. New Hepatitis C Infections Nearly Tripled Over Five Years: Deadly Virus Concentrated Among Baby Boomers and Increasingly Rapidly Among New Generations of Americans. Published 2017. Available at: <https://www.cdc.gov/nchhstp/newsroom/2017/Hepatitis-Surveillance-Press-Release.html>. Accessed February 10, 2020.
- ¹⁰³ Suryaprasad AG, White JZ, Xu F, Eichler BA, Hamilton J, Patel A, Hamdounia SB, Church DR, Barton K, Fisher C, Macomber K, Stanley M, Guilfoyle SM, Sweet K, Liu S, Iqbal K, Tohme R, Sharapov U, Kupronis BA, Ward JW, Holmberg SD. Emerging Epidemic of Hepatitis C Virus Infections Among Young Nonurban Persons who Inject Drugs in the United States, 2006-2012. Clinical Infectious Diseases. 2014;59:1411-9.
- ¹⁰⁴ Lemelin J, Hogg, W, Baskerville N. Evidence to Action: A Tailored Multifaceted Approach to Changing Family Physician Practice Patterns and Improving Preventive Care. Canadian Medical Association Journal. 2001;164:757-63.
- ¹⁰⁵ Figueiras A, Herdeiro MT, Polonia J, Gestal-Otero JJ. An Educational Intervention to Improve Physician Reporting of Adverse Drug Reactions: A Cluster Randomized Controlled Trial. JAMA 2006;296:1086-93.
- ¹⁰⁶ Avorn J, Soumerai SB, Everitt DE, Ross-Degnan D, Beers MH, Sherman D, Salem-Schatz SR, Fields D. A Randomized Trial of a Program to Reduce the Use of Psychoactive Drugs in Nursing Homes. The New England Journal of Medicine. 1992;327:168-73.
- ¹⁰⁷ Avorn J, Soumerai SB. Improving Drug-Therapy Decisions Through Educational Outreach. A Randomized Controlled Trial of Academically Based "Detailing". The New England Journal of Medicine. 1983;308:1457-63.
- ¹⁰⁸ Meisenberg BR, Grover J, Campbell C, Korpon D. Assessment of Opioid Prescribing Practices Before and After Implementation of a Health System Intervention to Reduce Opioid Overprescribing. JAMA Network Open. 2018;1:e182908.
- ¹⁰⁹ O'Brien MA, Rogers S, Jamtvedt G, Oxman AD, Odgaard-Jensen J, Kristoffersen DT, Forsetlund L, Bainbridge D, Freemantle N, Davis DA, Haynes RB, Harvey EL. Educational Outreach Visits: Effects on Professional Practice and Health Care Outcomes. The Cochrane Library. 2007;CD000409.
- ¹¹⁰ Grimshaw JM, Shirran L, Thomas R, Mowatt G, Fraser C, Bero L, Grilli R, Harvey E, Oxman A, O'Brien MA. Changing Provider Behavior: An Overview of Systematic Reviews of Interventions. Medical Care. 2001;39:II2- II45.

CONFIDENTIAL

-
- ¹¹¹ Losby JL, Hyatt JD, Kanter MH, Baldwin G, Matsuoka D. Safer and More Appropriate Opioid Prescribing: A Large Healthcare System's Comprehensive Approach. *Journal of Evaluation in Clinical Practice*. 2017;23:1173-9.
- ¹¹² Meisenberg BR, Grover J, Campbell C, Korpon D. Assessment of Opioid Prescribing Practices Before and After Implementation of a Health System Intervention to Reduce Opioid Overprescribing. *JAMA Network Open*. 2018;1:e182908.
- ¹¹³ Bounthavong M, Devine EB, Christopher ML, Harvey MA, Veenstra DL, Basu A. Implementation Evaluation of Academic Detailing on Naloxone Prescribing Trends at the United States Veterans Health Administration. *Health Services Research*. 2019;54:1055-64.
- ¹¹⁴ Losby JL, Hyatt JD, Kanter MH, Baldwin G, Matsuoka D. Safer and More Appropriate Opioid Prescribing: A Large Healthcare System's Comprehensive Approach. *Journal of Evaluation in Clinical Practice*. 2017;23:1173-9.
- ¹¹⁵ Bounthavong M, Devine EB, Christopher ML, Harvey MA, Veenstra DL, Basu A. Implementation Evaluation of Academic Detailing on Naloxone Prescribing Trends at the United States Veterans Health Administration. *Health Services Research*. 2019;54:1055-64.
- ¹¹⁶ Behar E, Rowe C, Santos GM, Santos N, Coffin PO. Academic Detailing Pilot for Naloxone Prescribing Among Primary Care Providers in San Francisco. *Family Medicine*. 2017;49:122-6.
- ¹¹⁷ Lin DH, Jones CM, Compton WM, Heyward J, Losby JL, Murimi IB, Baldwin GT, Ballreich JM, Thomas D, Bicket M, Porter L, Tierce JC, Alexander GC. Prescription Drug Coverage for Low Back Pain Among United States Medicaid, Medicare Advantage and Commercial Insurers. *JAMA Network Open*. 2018;1:e180235.
- ¹¹⁸ Chou R, Deyo R, Friedly J, Skelly A, Hashimoto R, Weimer M, Fu R, Dana T, Kraegel P, Griffin J, Grusing S. Nonpharmacologic Therapies for Low Back Pain: A Systematic Review for an American College of Physicians Clinical Practice Guideline. *Annals of Internal Medicine*. 2017;166:493-505.
- ¹¹⁹ Centers for Disease Control and Prevention. Pocket Guide: Tapering Opioids for Chronic Pain. Available at: https://www.cdc.gov/drugoverdose/pdf/clinical_pocket_guide_tapering-a.pdf. Accessed February 10, 2020.
- ¹²⁰ Oregon Pain Guidance. Tapering – Guidance & Tools. Published 2018. Available at: <https://www.oregonpainguidance.org/guideline/tapering>. Accessed February 10, 2020.
- ¹²¹ Berna C, Kulich RJ, Rathmell JP. Tapering Long-term Opioid Therapy in Chronic Noncancer Pain: Evidence and Recommendations for Everyday Practice. In *Mayo Clinic Proceedings*. 2015;90:828-42.
- ¹²² Powell VD, Rosenberg JM, Yaganti A, Garpestad C, Lagisetty P, Shannon C, Silveira MJ. Evaluation of Buprenorphine Rotation in Patients Receiving Long-term Opioids for Chronic Pain: A Systematic Review. *JAMA Network Open*. 2021;4(9):e2124152.
- ¹²³ Chang HY, Lyapustina T, Rutkow L, Daubresse M, Richey M, Faul M, Stuart EA, Alexander GC. Impact of Prescription Drug Monitoring Programs and Pill Mill Laws on High-Risk Opioid Prescribers: A Comparative Interrupted Time Series Analysis. *Drug and Alcohol Dependence*. 2016;165:1-8.
- ¹²⁴ Swedlow A, Ireland J, and Johnson G. Prescribing Patterns of Schedule II Opioids in California Workers' Compensation. Published 2011. Available at: <https://www.cwci.org/document.php?file=1438.pdf>. Accessed February 10, 2020.
- ¹²⁵ Mello MM, Messing NA. Restrictions on the Use of Prescribing Data for Drug Promotion. *The New England Journal of Medicine*. 2011;365:1248-54.
- ¹²⁶ Centers for Disease Control and Prevention. CDC Guideline for Prescribing Opioids for Chronic Pain. Published 2017. Available at: <https://www.cdc.gov/drugoverdose/prescribing/guideline.html>. Accessed March 4, 2019.
- ¹²⁷ Centers for Disease Control and Prevention. Process for Updating the Opioid Prescribing Guideline. Available at: <https://www.cdc.gov/opioids/guideline-update/index.html>. Accessed June 13, 2022.
- ¹²⁸ National Resource Center for Academic Detailing. Local Opioid Overdose Prevention Using Academic Detailing: Implementation Guide. Published 2019. Available at: https://www.narcad.org/uploads/5/7/9/5/57955981/ad_implementation_guide.pdf. Accessed April 14, 2021.

CONFIDENTIAL

-
- ¹²⁹ Navathe AS, Liao JM, Yan XS, Delgado MK, Isenberg WM, Landa HM, Bond BL, Small DS, Rareshide CAL, Shen Z, Pepe RS, Refai F, Lei VJ, Volpp KG, Patel MS. The Effect of Clinician Feedback Interventions on Opioid Prescribing. *Health Affairs*. 2022;41:424-433.
- ¹³⁰ Centers for Disease Control and Prevention. CDC Clinical Practice Guideline for Prescribing Opioids—United States, 2022. Published 2022. Available at: <https://downloads.regulations.gov/CDC-2022-0024-0002/content.pdf>. Accessed June 13, 2022.
- ¹³¹ Haddox JD, Joranson D, Angarola RT, Brady A, Carr DB, Blonsky ER, Burchiel K, Gitlin M, Midcap M, Payne R, Simon D, Vasudevan S, Wilson P. The Use of Opioids for the Treatment of Chronic Pain: A Consensus Statement from the American Academy of Pain Medicine and the American Pain Society. *The Clinical Journal of Pain*. 1997;13:6-8.
- ¹³² Centers for Disease Control and Prevention. CDC Guideline for Prescribing Opioids for Chronic Pain. Published 2017. Available at: <https://www.cdc.gov/drugoverdose/prescribing/guideline.html>. Accessed March 14, 2019.
- ¹³³ National Resource Center for Academic Detailing. Detailing Directory. Available at: <http://www.narcad.org/the-detailing-directory.html>. Accessed February 10, 2020.
- ¹³⁴ Alosa Health. Available at: <https://alosahealth.org>. Accessed February 10, 2020.
- ¹³⁵ Johnson CY. X. The Washington Post. Published 2019. Available at: https://www.washingtonpost.com/national/health-science/combating-the-opioid-crisis-one-doctor-at-a-time/2019/02/01/9d11c1a0-1a71-11e9-8813-cb9dec761e73_story.html. Accessed July 30, 2020.
- ¹³⁶ United States Drug Enforcement Agency. The Controlled Substances Act. Available at: <https://www.dea.gov/drug-information/csa>. Accessed August 5, 2022.
- ¹³⁷ Lo B, Ott C. What Is the Enemy in CME, Conflicts of Interest or Bias?. *JAMA*. 2013;310:1019-20.
- ¹³⁸ Sandbrink F, Uppal R. The Time for Opioid Stewardship Is Now. *Joint Commission Journal on Quality and Patient Safety*. 2019;45:1-2.
- ¹³⁹ Pharmaceutical Assistance Contract for the Elderly. Annual Report to the Pennsylvania General Assembly. Published 2017. Available at: <https://www.aging.pa.gov/publications/annual-reports/Documents/2017%20PACE%20Annual%20Report.pdf>. Accessed February 10, 2020.
- ¹⁴⁰ TOPCARE. Available at: <http://mytopcare.org>. Accessed February 10, 2020.
- ¹⁴¹ United States Department of Veterans Affairs. Pharmacy Benefits Management Services, Academic Detailing Service - About Us. Available at: <https://www.pbm.va.gov/PBM/academicdetailingservice/AboutUs.asp>. Accessed February 10, 2020.
- ¹⁴² Havens C. Academic Detailing at Kaiser Permanente Northern California. Published 2011. Available at: http://www.ehcca.com/presentations/compeffective3/havens_pc.pdf. Accessed February 10, 2020.
- ¹⁴³ O'Brien MA, Rogers S, Jamtvedt G, Oxman AD, Odgaard-Jensen J, Kristoffersen DT, Forsetlund L, Bainbridge D, Freemantle N, Davis DA, Haynes RB, Harvey EL. Educational Outreach Visits: Effects on Professional Practice and Health Care Outcomes. *The Cochrane Library*. 2007;CD000409.
- ¹⁴⁴ Dowell D, Haegerich TM, Chou R. Centers for Disease Control and Prevention (CDC) Guideline for Prescribing Opioids for Chronic Pain - United States, 2016. *JAMA*. 2016;315:1624-45.
- ¹⁴⁵ Department of Veterans Affairs, Department of Defense. VA/DoD Clinical Practice Guideline for Opioid Therapy for Chronic Pain Version 3.0. Published 2017. Available at: <https://www.healthquality.va.gov/guidelines/Pain/cot/VADoDOTCPG022717.pdf>. Accessed January 29, 2019.
- ¹⁴⁶ Centers for Disease Control and Prevention. Opioid Overdose: Helpful Materials for Patients. Published 2019. Available at: <https://www.cdc.gov/drugoverdose/patients/materials.html>. Accessed February 10, 2020.
- ¹⁴⁷ United States Department of Health & Human Services, Substance Abuse and Mental Health Services Administration. Opioid Overdose Prevention Toolkit. Published 2018. Available at: <https://store.samhsa.gov/product/Opioid-Overdose-Prevention-Toolkit/SMA18-4742>. Accessed February 10, 2020.

CONFIDENTIAL

-
- ¹⁴⁸ American College of Surgeons. Patient Education Initiatives, Safe Pain Control: Opioid Abuse and Surgery. Available at: <https://www.facs.org/education/opioids/patient-ed>. Accessed February 10, 2020.
- ¹⁴⁹ Heath C, Heath D. Made to Stick: Why Some Ideas Survive and Others Die. Random House, New York, New York, 2007.
- ¹⁵⁰ Hornik R, Maklan D, Cadell D, Prado A, Barmada C, Jacobsohn L, Orwin Robert, Sridharan S, Zador P, Southwell B, Zanutto E, Baskin R, Chu A, Morin C, Talyor K, Steele D. Evaluation of the National Youth Anti-Drug Media Campaign: Fourth Semi-Annual Report of Findings. Published 2002. Available at: http://www.emcdda.europa.eu/attachements.cfm/att_94030_EN_NIDA%20mass%20media%20campaign%20eval. Accessed February 10, 2020.
- ¹⁵¹ Wakefield MA, Loken B, Hornik RC. Use of Mass Media Campaigns to Change Health Behaviour. The Lancet. 2010;376:1261-71.
- ¹⁵² Allara E, Ferri M, Bo A, Gasparrini A, Faggianov F. Are Mass-Media Campaigns Effective in Preventing Drug Use? A Cochrane Systematic Review and Meta-Analysis. BMJ Open. 2015;5:e007449.
- ¹⁵³ Christie C, Baker C, Cooper R, Kennedy PJ, Madras B, Bondi B. The President's Commission on Combating Drug Addiction and the Opioid Crisis. Published 2017. Available at: https://www.whitehouse.gov/sites/whitehouse.gov/files/images/Final_Report_Draft_11-1-2017.pdf. Accessed November 27, 2018.
- ¹⁵⁴ Farrelly MC, Duke JC, Nonnemaker J, MacMonegle AJ, Alexander TN, Zhao X, Delahanty JC, Rao P, Allen JA. Association Between the Real Cost Media Campaign and Smoking Initiation Among Youths – United States, 2014–2016. Morbidity and Mortality Weekly Report. 2017;66:47-50.
- ¹⁵⁵ Duke JC, Woodlea R, Arnold KY, MacMonegle AJ, Nonnemaker JM, Porter L. Effect of a Statewide Media Campaign on Smoking Cessation Among Florida Adults. Preventing Chronic Disease. 2020;17:190271.
- ¹⁵⁶ Substance Abuse and Mental Health Services Administration, Center for the Application of Prevention Technologies. Media Campaigns to Prevent Prescription Drug and Opioid Misuse. Published 2017. Available at: <https://iseralaska.org/static/akpfs/media-campaigns-prevent-rx-drugs-opioid-misuse.pdf>. Accessed February 10, 2020.
- ¹⁵⁷ Substance Abuse and Mental Health Services Administration, Center for the Application of Prevention Technologies. Getting the Message Right! Considerations for Media Campaigns to Prevent Opioid Misuse and Overdose (Webinar Summary). Published 2017. Available at: <https://mnprc.org/wp-content/uploads/2019/01/nmupd-media-campaigns-summary.pdf>. Accessed July 25, 2022.
- ¹⁵⁸ State of New Jersey, Department of Human Services. ReachNJ. Available at: <https://reachnj.gov>. Accessed December 30, 2020.
- ¹⁵⁹ Jennings K. Christie's Yearlong Opioid Advertising Campaign Tops \$42M. Published 2018. Available at: <https://www.politico.com/states/new-jersey/story/2018/01/05/christies-yearlong-opioid-advertising-campaign-tops-42m-172696>. Accessed March 17, 2020.
- ¹⁶⁰ Centers for Disease Control and Prevention. Addressing the Prescription Opioid Crisis. CDC Rx Awareness Campaign Overview. Published 2017. Available at: <https://www.cdc.gov/rxawareness/pdf/Overview-Rx-Awareness-Resources.pdf>. Accessed March 17, 2020.
- ¹⁶¹ Substance Abuse and Mental Health Services Administration, Center for the Application of Prevention Technologies. Getting the Message Right! Considerations for Media Campaigns to Prevent Opioid Misuse and Overdose (Webinar Transcript). Published 2017. Available at: <https://iseralaska.org/static/akpfs/nmupd-webinar-series-part-1-transcript.pdf>. Accessed July 25, 2022.
- ¹⁶² Rath JM, Perks SN, Vallone DM, Barton AA, Stephens DK, Simard B, Hair EC. Educating Young Adults About Opioid Misuse: Evidence from a Mass Media Intervention. International Journal of Environmental Research and Public Health. 2021;19:22.
- ¹⁶³ Olsen Y, Sharfstein JM. Confronting the Stigma of Opioid Use Disorder – and its Treatment. JAMA. 2014;311:1393-4.

CONFIDENTIAL

-
- ¹⁶⁴ Kennedy-Hendricks A, Gielen AC, McGinty EE, McDonald E, Shields W, Barry CL. Medication Sharing, Storage, and Disposal Practices for Opioid Medications Among United States Adults. *JAMA Intern Med.* 2016;176:1027-9.
- ¹⁶⁵ Seamans MJ, Carey TS, Westreich DJ, Cole SR, Wheeler SB, Alexander GC, Pate V, Brookhart MA. Association of Household Opioid Availability and Prescription Opioid Initiation Among Household Members. *JAMA Intern Med.* 2018;178:102-9.
- ¹⁶⁶ Nguyen AP, Glanz JM, Narwaney KJ, Binswanger IA. Association of Opioids Prescribed to Family Members with Opioid Overdose Among Adolescents and Young Adults. *JAMA Network Open.* 2020;3:e201018.
- ¹⁶⁷ Bicket MC, Long JJ, Pronovost PJ, Alexander GC, Wu CL. Prescription Opioid Analgesics Commonly Unused After Surgery: A Systematic Review. *JAMA Surgery.* 2017;152:1066-71.
- ¹⁶⁸ National Academies of Sciences, Engineering, and Medicine. Pain Management and the Opioid Epidemic: Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use. Washington, DC: National Academies Press. 2017;5:317-9.
- ¹⁶⁹ Seehusen DA, Edwards J. Patient Practices and Beliefs Concerning Disposal of Medications. *Journal of the American Board of Family Medicine.* 2006;19:542-7.
- ¹⁷⁰ McCance-Katz EF. The National Survey on Drug Use and Health: 2017. Available at: <https://www.samhsa.gov/data/sites/default/files/nsduh-ppt-09-2018.pdf>. Accessed February 10, 2020.
- ¹⁷¹ United States Food and Drug Administration. Disposal of Unused Medicines: What You Should Know. Published 2019. Available at: <https://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/EnsuringSafeUseofMedicine/SafeDisposalofMedicines/ucm186187.htm>. Accessed February 10, 2020.
- ¹⁷² Executive Office of the President of the United States. National Drug Control Policy, 2011. Available at: <https://obamawhitehouse.archives.gov/sites/default/files/ondcp/ndcs2011.pdf>. Accessed February 10, 2020.
- ¹⁷³ United States Drug Enforcement Agency. 21th National Take Back Day. Available at: <https://www.dea.gov/sites/default/files/2022-01/NTBDI-Results-october%202021.pdf>. Accessed March 7, 2022.
- ¹⁷⁴ Rogers DS, Tibben-Lembke RS. Going Backwards: Reverse Logistics Trends and Practices. Pittsburgh, PA: Reverse Logistics Executive Council. 1998.
- ¹⁷⁵ Thach AV, Brown CM, Pope N. Consumer Perceptions About a Communities Pharmacy-Based Medication Take Back Program. *Journal of Environmental Management.* 2013;127:23-7.
- ¹⁷⁶ United States Government Accountability Office. Low Participation by Pharmacies and Other Entities as Voluntary Collectors of Unused Prescription Drugs. Published 2017. Available at: <https://www.gao.gov/assets/690/687719.pdf>. Accessed February 10, 2020.
- ¹⁷⁷ Egan KL, Gregory E, Sparks M, Wolfson M. From Dispensed to Disposed: Evaluating the Effectiveness of Disposal Programs through a Comparison with Prescription Drug Monitoring Program Data. *The American Journal of Drug and Alcohol Abuse.* 2017;43:69-77.
- ¹⁷⁸ United States Food and Drug Administration. Disposal of Unused Medicines: What You Should Know. Published 2019. Available at: <https://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/EnsuringSafeUseofMedicine/SafeDisposalofMedicines/ucm186187.htm>. Accessed February 10, 2020.
- ¹⁷⁹ DisposeRx. Available at: <https://disposerx.com>. Accessed February 10, 2020.
- ¹⁸⁰ Product Stewardship Institute. How-To Guide for Drug Take-Back: Managing a Pharmacy-Based Collection Program for Leftover Household Pharmaceuticals. Published 2016. Available at: https://www.productstewardship.us/page/Start_Drug_Takeback. Accessed February 10, 2020.

CONFIDENTIAL

-
- ¹⁸¹ King County. 2017 King County, Washington, MED-Project Annual Report. Published 2018. Available at: <https://kingcountysecuremedicinereturn.org/wp-content/uploads/2018/10/22-med-project-2017-annual-report-king-county-07-17-2018.pdf>. Accessed February 10, 2020.
- ¹⁸² Product Stewardship Institute. How-To Guide for Drug Take-Back: Managing a Pharmacy-Based Collection Program for Leftover Household Pharmaceuticals. Published 2016. Available at: https://www.productstewardship.us/page/Start_Drug_Takeback. Accessed February 10, 2020.
- ¹⁸³ Winchester Virginia Police Department. Medication Disposal. Available at: <https://www.winchesterpolice.org/services/medication-disposal>. Accessed February 10, 2020.
- ¹⁸⁴ Burris S. Syringe Possession Laws Report. Published 2017. Available at: <http://lawatlas.org/datasets/paraphernalia-laws>. Accessed February 15, 2020.
- ¹⁸⁵ The Center for Community Solutions. Ohio Syringe Services Program Profiles. Available at https://www.communitysolutions.com/wp-content/uploads/2019/05/IssueBrief_Ohio-Syringe-Services-Program-Profiles_SSobul_updated-05202019.pdf. Accessed December 4, 2020.
- ¹⁸⁶ Tilson H, Aramrattana A, Bozzette S, Celentano D, Falco M, Hammett T, Kozlov A, Lai S, Mahal A, Schottenfeld R. Preventing HIV Infection Among Injecting Drug Users in High Risk Countries: An Assessment of the Evidence. Washington, DC: Institute of Medicine. Published 2007. Available at: <https://www.nap.edu/catalog/11731/preventing-hiv-infection-among-injecting-drug-users-in-high-risk-countries>. Accessed February 15, 2020.
- ¹⁸⁷ Lenton S, Single E. The Definition of Harm Reduction. *Drug and Alcohol Review*. 1998;17:213-9.
- ¹⁸⁸ Global Commission on Drug Policy. War on Drugs: Report of the Global Commission on Drug Policy. Published 2011. Available at: https://www.scribd.com/fullscreen/56924096?access_key=key-xoixompyejnky70a9mq. Accessed February 15, 2020.
- ¹⁸⁹ Shultz GP, Aspe P. The Failed War on Drugs. Published 2017. Available at: <https://www.nytimes.com/2017/12/31/opinion/failed-war-on-drugs.html>. Accessed February 15, 2020.
- ¹⁹⁰ Caulkins JP, Reuter P. How Drug Enforcement Affects Drug Prices. *Crime and Justice*. 2010;39:213-71.
- ¹⁹¹ Pollack HA, Reuter P. Does Tougher Enforcement Make Drugs More Expensive?. *Addiction*. 2014;109:1959-66.
- ¹⁹² Werb D, Rowell G, Guyatt G, Kerr T, Montaner J, Wood E. Effect of Drug Law Enforcement on Drug Market Violence: A Systematic Review. *International Journal of Drug Policy*. 2011;22:87-94.
- ¹⁹³ Centers for Disease Control and Prevention. Injection Drug Use and HIV Risk. Published 2020. Available at: http://www.cdc.gov/idu/pubs/hiv_prev.htm. Accessed February 15, 2020.
- ¹⁹⁴ Bluthenthal RN, Kral AH, Gee L, Erringer EA, Edlin BR. The Effect of Syringe Exchange Use on High-Risk Injection Drug Users: A Cohort Study. *AIDS*. 2000;14:605-11.
- ¹⁹⁵ Singer M, Himmelgreen D, Weeks MR, Radda KE, Martinez R. Changing the Environment of AIDS Risk: Findings on Syringe Exchange and Pharmacy Sales of Syringes in Hartford, CT. *Medical Anthropology*. 1997;18:107-30.
- ¹⁹⁶ Hagan H, Jarlais DC, Friedman SR, Purchase D, Alter MJ. Reduced Risk of Hepatitis B and Hepatitis C Among Injection Drug Users in the Tacoma Syringe Exchange Program. *American Journal of Public Health*. 1995;85:1531-7.
- ¹⁹⁷ Des Jarlais DC, Marmor M, Paone D. HIV Incidence Among Injecting Drug Users in New York City Syringe Exchange Programs. *Lancet*. 1996;348:987-91.
- ¹⁹⁸ Hurley SF, Jolley DJ, Kaldor JM. Effectiveness of Needle Exchange Programmes for Prevention of HIV Infection. *Lancet*. 1997;349:1797-1800.
- ¹⁹⁹ Abdul-Quader AS, Feelemyer J, Modi S, Stein ES, Briceno A, Semaan S, Horvath T, Kennedy GE, Des Jarlais DC. Effectiveness of Structural-Level Needle/Syringe Programs to Reduce HCV and HIV Infection Among People Who Inject Drugs: A Systematic Review. *AIDS and Behavior*. 2013;17:2878-92.

CONFIDENTIAL

-
- ²⁰⁰ Wodak A, Cooney A. Do Needle Syringe Programs Reduce HIV Infection Among Injecting Drug Users: A Comprehensive Review of the International Evidence. *Substance Use & Misuse*. 2006;41:777-813.
- ²⁰¹ Hagan H, Des Jarlais DC, Friedman SR, Purchase D, Amaro H. Reduced Risk of Hepatitis B and Hepatitis C Among Injection Drug Users in the Tacoma Syringe Exchange Program. *Am J Public Health* 1995;85:1531-7.
- ²⁰² National Institutes of Health. Interventions to Prevent HIV Risk Behaviors. Consensus Development Conference Statement. 1997;15:1-41.
- ²⁰³ Aspinall EJ, Nambiar D, Goldberg DJ, Hickman M, Weir A, Van Velzen E, Palmateer N, Doyle JS, Hellard ME, Hutchinson SJ. Are Needle and Syringe Programmes Associated with a Reduction in HIV Transmission Among People Who Inject Drugs: A Systematic Review and Meta-Analysis. *International Journal of Epidemiology*. 2014;43:235-48.
- ²⁰⁴ Nacopoulos AG, Lewtas AJ, Ousterhout MM. Syringe Exchange Programs: Impact on Injection Drug Users and the Role of the Pharmacist from a United States Perspective. *Journal of the American Pharmacists Association*. 2010;50:148-57.
- ²⁰⁵ Clarke K, Harris D, Zweifler JA, Lasher M, Mortimer RB, Hughes S. The Significance of Harm Reduction as a Social and Health Care Intervention for Injecting Drug Users: An Exploratory Study of a Needle Exchange Program in Fresno, California. *Soc Work Public Health*. 2016;31:398-407.
- ²⁰⁶ North American Syringe Exchange Network (NASEN). Directory of Syringe Exchange Programs. Available at: <https://www.nasen.org>. Accessed February 15, 2020.
- ²⁰⁷ Paraskos B, Hickinbotham L, Hill R, Sheridan D. Correcting Misconceptions About Syringe Service Programs. *Nursing* 2020. 2019;49:62-3.
- ²⁰⁸ Marx MA, Crape B, Brookmeyer RS, Junge B, Latkin C, Vlahov D, Strathdee SA. Trends in Crime and the Introduction of a Needle Exchange Program. *American Journal of Public Health*. 2000;90:1933.
- ²⁰⁹ Galea S, Ahern J, Fuller CM, Freudenberg N, Vlahov D. Needle Exchange Programs and Experience of Violence in an Inner City Neighborhood. *Journal of Acquired Immune Deficiency Syndromes*. 2001;28:282-8.
- ²¹⁰ Tinsman PD, Bullman S, Chen X, Burgdorf K, Herrell JM. Factors Affecting Client Response to HIV Outreach Efforts. *Journal of Substance Abuse*. 2001;13:201-14.
- ²¹¹ Kennedy MC, Karamouzian M, Kerr T. Public Health and Public Order Outcomes Associated with Supervised Drug Consumption Facilities: A Systematic Review. *Current HIV/AIDS reports*. 2017;14:161-83.
- ²¹² Marshall BD, Milloy MJ, Wood E, Montaner JS, Kerr T. Reduction in Overdose Mortality after the Opening of North America's First Medically Supervised Safer Injecting Facility: A Retrospective Population-Based Study. *Lancet*. 2011;377:1429-37.
- ²¹³ Stoltz JA, Wood E, Small W, Li K, Tyndall M, Montaner J, Kerr T. Changes in Injecting Practices Associated with the Use of a Medically Supervised Safer Injection Facility. *Journal of Public Health*. 2007;29:35-9.
- ²¹⁴ Wood E, Tyndall MW, Montaner JS, Kerr T. Summary of Findings from the Evaluation of a Pilot Medically Supervised Safer Injecting Facility. *CMAJ*. 2006;175:1399-1404.
- ²¹⁵ 5 Things to Know About Overdose Prevention Sites. Hopkins Bloomberg Public Health Magazine. Published 2019. Available at: <https://magazine.jhsph.edu/2019/5-things-know-about-overdose-prevention-sites>. Accessed June 15, 2021.
- ²¹⁶ Otter D. Safe Consumption Facilities: Evidence and Models. Available at: https://kingcounty.gov/~media/depts/community-human-services/behavioral-health-recovery/documents/herointf/Safe_Consumption_Facilities_Evidence_Models.ashx?la=en. Accessed March 5, 2019.
- ²¹⁷ Armbrrecht E, Guzauskas G, Hansen R, Pandey R, Fazioli K, Chapman R, Pearson SD, Rind DM. Supervised Injection Facilities and Other Supervised Consumption Sites: Effectiveness and Value; Final Evidence Report. Institute for Clinical and Economic Review. Published 2021. Available at: https://icer.org/wp-content/uploads/2020/10/ICER_SIF_Final-Evidence-Report_010821.pdf. Accessed July 25, 2022.
- ²¹⁸ Potier C, Laprevote V, Dubois-Arber F, Cottencin O, Rolland B. Supervised Injection Services: What has Been Demonstrated? A Systematic Literature Review. *Drug Alcohol Depend*. 2014;145:48-68.

CONFIDENTIAL

-
- ²¹⁹ Hedrich D. European Report on Drug Consumption Rooms. European Monitoring Centre for Drugs and Drug Addiction. 2004.
- ²²⁰ Dubois-Arber F, Benninghoff F, Jeannin A. Typology of Injection Profiles of Clients of a Supervised Drug Consumption Facility in Geneva, Switzerland. *Eur Addict Res.* 2008;14:1-10.
- ²²¹ Kinnard EN, Howe CJ, Kerr T, Hass VS, Marshall BD. Self-Reported Changes in Drug Use Behaviors and Syringe Disposal Methods Following the Opening of a Supervised Injecting Facility in Copenhagen, Denmark. *Harm Reduction Journal.* 2014;11:29.
- ²²² Armbrecht E, Guzauskas G, Hansen R, Pandey R, Fazioli K, Chapman R, Pearson SD, Rind DM. Supervised Injection Facilities and Other Supervised Consumption Sites: Effectiveness and Value; Final Evidence Report. Institute for Clinical and Economic Review. Published 2021. Available at: https://icer.org/wp-content/uploads/2020/10/ICER_SIF_Final-Evidence-Report_010821.pdf. Accessed July 25, 2022.
- ²²³ Drug Policy Alliance. Overdose Prevention Centers. Available at: <https://drugpolicy.org/issues/supervised-consumption-services>. Accessed July 25, 2022.
- ²²⁴ O'Donnell JK, Halpin J, Matson CL, Goldberger BA, Gladden, R Matthew. Deaths Involving Fentanyl, Fentanyl Analogs, and U-47700 – 10 States, July–December 2016. *Morbidity and Mortality Weekly Report.* 2017;3:1197-1202.
- ²²⁵ Drug Enforcement Administration (DEA) Strategic Intelligence Section. National Heroin Threat Assessment Summary - Updated. Published 2016. Available at: https://www.dea.gov/sites/default/files/2018-07/hq062716_attach.pdf. Accessed February 15, 2020.
- ²²⁶ The New York State Department of Health AIDS Institute. Fentanyl: The 411. Available at: <https://www.health.ny.gov/publications/9971.pdf>. Accessed March 7, 2022.
- ²²⁷ Mars SG, Ondocsin J, Ciccarone D. Sold as Heroin: Perceptions and Use of an Evolving Drug in Baltimore, MD. *Journal of Psychoactive Drugs.* 2018;50:167-76.
- ²²⁸ Larnder A, Saatchi A, Borden SA, Moa B, Gill CG, Wallace B, Hore D. Variability in the Unregulated Opioid Market in the Context of Extreme Rates of Overdose. *Drug and Alcohol Dependence.* 2022;235:109427.
- ²²⁹ Bloomberg American Health Initiative. Detecting Fentanyl, Saving Lives. Available at: <https://americanhealth.jhu.edu/fentanyl/>. Accessed February 15, 2020.
- ²³⁰ King K. Drug Users Interested in Cheap Test Strips That Can Detect Deadly Fentanyl. Published 2018. Available at: <https://wtop.com/science/2018/02/test-strips-fentanyl/>. Accessed February 15, 2020.
- ²³¹ Karamouzian M, Dohoo C, Forsting S, McNeil R, Kerr T, Lysyshyn M. Evaluation of a Fentanyl Drug Checking Service for Clients of a Supervised Injection Facility, Vancouver, Canada. *Harm Reduction Journal.* 2018;15:1-8.
- ²³² Peiper NC, Clarke SD, Vincent LB, Ciccarone D, Kral AH, Zibbell JE. Fentanyl Test Strips as an Opioid Overdose Prevention Strategy: Findings from a Syringe Services Program in the Southeastern United States. *International Journal of Drug Policy.* 2019;63:122-8.
- ²³³ Karamouzian M, Dohoo C, Forsting S, McNeil R, Kerr T, Lysyshyn M. Evaluation of a Fentanyl Drug Checking Service for Clients of a Supervised Injection Facility, Vancouver, Canada. *Harm Reduct J.* 2018;15:46.
- ²³⁴ Sherman SG, Morales KB, Park JN, McKenzie M, Marshall BD, Green TC. Acceptability of Implementing Communities-Based Drug Checking Services for People Who Use Drugs in Three United States Cities: Baltimore, Boston and Providence. *International Journal of Drug Policy.* 2019;68:46-53.
- ²³⁵ Ohio Department of Health. Project DAWN / Summit Safe Program Statistics. Available at: <https://app.powerbi.com/view?r=eyJrIjojNTIzYjYjBIMzAtN2Q4YS00M2NiLWFmNmEtNDEyYzc3NzA1MTg4IiwidCI6ImJiMWI0YjU2LTQ4N2EtNGIyMy04YTl0LWEzYWVmNjVIMTFmZiIsImMiOiJF9>. Accessed December 4, 2020.
- ²³⁶ Haffajee RL, Jena AB, Weiner SG. Mandatory Use of Prescription Drug Monitoring Programs. *JAMA.* 2015;313:891-2.
- ²³⁷ Centers for Disease Control and Prevention. Prescription Drug Monitoring Programs (PDMPs). Available at: <https://www.cdc.gov/opioids/providers/pdmps.html>. Accessed March 9, 2022.

CONFIDENTIAL

-
- ²³⁸ Haegerich TM, Paulozzi LJ, Manns BJ, Jones CM. What We Know, and Don't Know, About the Impact of State Policy and Systems-Level Interventions on Prescription Drug Overdose. *Drug Alcohol Depend.* 2014;145:34-47.
- ²³⁹ Rutkow L, Chang HY, Daubresse M, Webster DW, Stuart EA, Alexander GC. Effect of Florida's Prescription Drug Monitoring Program and Pill Mill Laws on Opioid Prescribing and Use. *JAMA Internal Medicine.* 2015;175:1642-9.
- ²⁴⁰ Patrick SW, Fry CE, Jones TF, Buntin MB. Implementation of Prescription Drug Monitoring Programs Associated with Reductions in Opioid-Related Death Rates. *Health Affairs.* 2016;35:1324-32.
- ²⁴¹ Prescription Behavior Surveillance System, Brandeis University. PBSS Data Brief Decline in Patient Prescription Risk Measures in Florida, 2011-2015. Published 2016. Available at: <https://www.floridahealth.gov/statistics-and-data/e-forcse/news-reports/documents/PBSS-data-brief.pdf>. Accessed July 25, 2022.
- ²⁴² Bao Y, Pan Y, Taylor A, Radakrishnan S, Luo F, Pincus HA, Schackman BR. Prescription Drug Monitoring Programs Are Associated with Sustained Reductions in Opioid Prescribing by Physicians. *Health Affairs.* 2016;35:1045-51.
- ²⁴³ Patrick SW, Fry CE, Jones TF, Buntin MB. Implementation of Prescription Drug Monitoring Programs Associated with Reductions in Opioid-Related Death Rates. *Health Affairs.* 2016;35:1324-32.
- ²⁴⁴ Wen H, Hockenberry JM, Jeng PJ, Bao Y. Prescription Drug Monitoring Program Mandates: Impact on Opioid Prescribing and Related Hospital Use. *Health Affairs.* 2019;38:1550-1556.
- ²⁴⁵ Substance Abuse and Mental Health Services Administration. Prescription Drug Monitoring Programs: A Guide for Healthcare Providers. In Brief, Volume 10, Issue 1. Published 2017. Available at: <https://store.samhsa.gov/sites/default/files/d7/priv/sma16-4997.pdf>. Accessed July 25, 2022.
- ²⁴⁶ Sacco L, Duff JH, Sarata AK. Prescription Drug Monitoring Programs. Congressional Research Service (CRS) Report for Congress, R42593. Published 2018. Available at: <https://sgp.fas.org/crs/misc/R42593.pdf>. Accessed July 25, 2022.
- ²⁴⁷ Centers for Disease Control and Prevention. Prescription Drug Monitoring Programs (PDMPs). Available at: <https://www.cdc.gov/opioids/providers/pdmps.html>. Accessed March 10, 2022.
- ²⁴⁸ Substance Abuse and Mental Health Services Administration. Prescription Drug Monitoring Programs: A Guide for Healthcare Providers. In Brief, Volume 10, Issue 1. Published 2017. Available at: <https://store.samhsa.gov/sites/default/files/d7/priv/sma16-4997.pdf>. Accessed July 25, 2022.
- ²⁴⁹ Neprash HT, Vock DM, Hanson A, Elert B, Short S, Karaca-Mandic P, Rothman AJ, Melton GB, Satin D, Markowitz R, Golberstein E. Effect of Integrating Access to a Prescription Drug Monitoring Program Within the Electronic Health Record on the Frequency of Queries by Primary Care Clinicians: A Cluster Randomized Clinical Trial. *JAMA Health Forum.* 2022;3:e221852.
- ²⁵⁰ Boté SH. U.S. Opioid Epidemic: Impact on Public Health and Review of Prescription Drug Monitoring Programs (PDMPs). *Online Journal of Public Health Informatics.* 2019;11:e18.
- ²⁵¹ Centers for Disease Control and Prevention. Prescription Drug Monitoring Programs (PDMPs). Available at: <https://www.cdc.gov/drugoverdose/pdmp/index.html>. Accessed March 10, 2022.
- ²⁵² Mihalic S, Fagan A, Irwin K, Ballard D, Elliott D. Blueprints for Violence Prevention (NCJ 204274). Washington, DC: Office of Juvenile and Delinquency Prevention. Published 2004. Available at: <https://www.ojp.gov/pdffiles1/ojdp/204274.pdf>. Accessed July 25, 2022.
- ²⁵³ Weissberg RP, Kumpfer KL, Seligman ME. Prevention that Works for Children and Youth. An Introduction. *Am Psychol.* 2003;58:425-32.
- ²⁵⁴ Sherman LW, Farrington DP, Welsh BC, MacKenzie DL. Evidence-Based Crime Prevention. *Preventing Crime: What Works for Children, Offenders, Victims and Places.* Dordrecht, The Netherlands: Springer. 2006;17.
- ²⁵⁵ Chou CP, Montgomery S, Pentz MA, Rohrbach LA, Johnson CA, Flay BR, MacKinnon DP. *Am J Public Health.* 1998; 88:944-8.
- ²⁵⁶ Botvin GJ, Baker E, Dusenbury L, Botvin EM, Diaz T. Long-Term Follow-Up Results of a Randomized Drug Abuse Prevention Trial in a White Middle-Class Population. *JAMA.* 1995;273:1106-12.

CONFIDENTIAL

- ²⁵⁷ Butterfoss FD, Goodman RM, Wandersman A. Community Coalitions for Prevention and Health Promotion. *Health Educ Res.* 1993;8:315-30.
- ²⁵⁸ Wandersman A. Community Science: Bridging the Gap Between Science and Practice with Community-Centered Models. *Am J Communities Psychol.* 2003;31:227-42.
- ²⁵⁹ The Center for Communities That Care. CTC PLUS. Available at: <https://www.communitiesthatcare.net/programs/ctc-plus/>. Accessed April 15, 2021.
- ²⁶⁰ Hawkins JD, Catalano RF, Arthur MW, Egan E, Brown EC, Abbott RD, Murray DM. Testing Communities that Care: The Rationale, Design and Behavioral Baseline Equivalence of the Community Youth Development Study. *Prevention Science.* 2008;9:178.
- ²⁶¹ Hawkins JD, Oesterle S, Brown EC, Monahan KC, Abbott RD, Arthur MW, Catalano RF. Sustained Decreases in Risk Exposure and Youth Problem Behaviors after Installation of the Communities That Care Prevention System in a Randomized Trial. *Archives of Pediatrics & Adolescent Medicine.* 2012;166:141-8.
- ²⁶² Hawkins JD, Oesterle S, Brown EC, Abbott RD, Catalano RF. Youth Problem Behaviors 8 Years After Implementing the Communities That Care Prevention System: A Community-Randomized Trial. *JAMA pediatrics.* 2014;168:122-9.
- ²⁶³ Hawkins JD, Oesterle S, Brown EC, Monahan KC, Abbott RD, Arthur MW, Catalano RF. Sustained Decreases in Risk Exposure and Youth Problem Behaviors after Installation of the Communities That Care Prevention System in a Randomized Trial. *Archives of Pediatrics & Adolescent Medicine.* 2012;166:141-8.
- ²⁶⁴ Hawkins JD, Oesterle S, Brown EC, Abbott RD, Catalano RF. Youth Problem Behaviors 8 Years After Implementing the Communities That Care Prevention System: A Community-Randomized Trial. *JAMA Pediatrics.* 2014;168:122-9.
- ²⁶⁵ Oesterle S, Hawkins JD, Kuklinski MR, Fagan AA, Fleming C, Rhew IC, Brown EC, Abbott RD, Catalano RF. Effects of Communities That Care on Males' and Females' Drug Use and Delinquency 9 years after Baseline in a Community-Randomized Trial. *American Journal of Community Psychology.* 2015;56:217-28.
- ²⁶⁶ Oesterle S, Hawkins JD, Kuklinski MR, Fagan AA, Fleming C, Rhew IC, Brown EC, Abbott RD, Catalano RF. Effects of Communities That Care on Males' and Females' Drug Use and Delinquency 9 Years After Baseline in a Community-Randomized Trial. *American Journal of Community Psychology.* 2015;56:217-28.
- ²⁶⁷ Hawkins JD, Oesterle S, Brown EC, Abbott RD, Catalano RF. Youth Problem Behaviors 8 Years After Implementing the Communities That Care Prevention System: A Community-Randomized Trial. *JAMA pediatrics.* 2014;168:122-9.
- ²⁶⁸ Communities That Care. Available at: <https://youth.gov/content/communities-care>. Accessed May 3, 2020.
- ²⁶⁹ Kuklinski MR, Briney JS, Hawkins JD, Catalano RF. Cost-Benefit Analysis of Communities That Care Outcomes at Eighth Grade. *Prevention Science.* 2012;13:150-61.
- ²⁷⁰ Kuklinski MR, Fagan AA, Hawkins JD, Briney JS, Catalano RF. Benefit-Cost Analysis of a Randomized Evaluation of Communities That Care: Monetizing Intervention Effects on the Initiation of Delinquency and Substance Use Through Grade 12. *J Exp Criminol.* 2015;11:165-92.
- ²⁷¹ United States Department of Human and Health Services. 5-Point Strategy to Combat the Opioid Crisis. Published 2018. Available at: <https://www.hhs.gov/opioids/about-the-epidemic/hhs-response/index.html>. Accessed February 15, 2020.
- ²⁷² Saloner B, Alvanzo A, Latimore A, Sharfstein J, Sherman S, Webster D. Ten Standards of Care: Policing and the Opioid Crisis. Published 2018. Available at: http://americanhealth.jhu.edu/sites/default/files/inline-files/PolicingOpioidCrisis_LONG_final_0.pdf. Accessed February 15, 2020.
- ²⁷³ Anderson TL, Donnelly EA, Delcher C, Wang Y. Data Science Approaches in Criminal Justice and Public Health Research: Lessons Learned From Opioid Projects. *Journal of Contemporary Criminal Justice.* 2021;37:175-91.
- ²⁷⁴ Center for Drug and Health Studies – University of Delaware. Delaware Opioid Metric Intelligence Project. Available at: <https://www.cdhs.udel.edu/projects/domip>. Accessed July 22, 2022.
- ²⁷⁵ Anderson TL, Donnelly EA, Delcher C, Wang Y. Data Science Approaches in Criminal Justice and Public Health Research: Lessons Learned From Opioid Projects. *Journal of Contemporary Criminal Justice.* 2021;37:175-91.

CONFIDENTIAL

-
- ²⁷⁶ Wang Y, Goldberger BA, Shin E, Delcher C. Florida Drug-Related Outcomes Surveillance and Tracking System (FROST). University of Florida. Available at: https://public.tableau.com/views/FloridaDrug-RelatedOutcomesSurveillanceandTrackingSystem_16370192338000/Home?:embed=y&:display_count=no&:showVizHome=no#1. Accessed July 22, 2022.
- ²⁷⁷ Berkowitz E and Jenkins D. Spotlight: Rhode Island's Cross-Agency Analysis on the Overdose and Addiction Crisis. Actionable Intelligence for Social Policy. Published 2021. Available at: <https://aisp.upenn.edu/wp-content/uploads/2021/09/AISP-Rhode-Island-Spotlight-FINAL.pdf>. Accessed July 22, 2022.
- ²⁷⁸ Rhode Island Executive Office of Health and Human Services. About the Ecosystem. Available at: <https://eohhs.ri.gov/initiatives/data-ecosystem>. Accessed July 22, 2022.
- ²⁷⁹ Berkowitz E and Jenkins D. SPOTLIGHT: Rhode Island's Cross-agency Analysis on the Overdose and Addiction Crisis. Actionable Intelligence for Social Policy. Published 2021. Available at: <https://aisp.upenn.edu/wp-content/uploads/2021/09/AISP-Rhode-Island-Spotlight-FINAL.pdf>. Accessed July 22, 2022.
- ²⁸⁰ Macmadu A, Paull K, Youssef R, Batthala S, Wilson KH, Samuels EA, Yedinak JL, Marshall BDL. Predictors of Enrollment in Opioid Agonist Therapy After Opioid Overdose or Diagnosis with Opioid Use Disorder: A Cohort Study. Drug and Alcohol Dependence. 2021;219:108435.
- ²⁸¹ Morrow JB, Roper-Miller JD, Catlin ML, Winokur AD, Cadwallader AB, Staymates JL, Williams SR, McGrath JG, Logan BK, McCormick MM, Nolte KB, Gilson TP, Menendez MJ, Goldberger BA. The Opioid Epidemic: Moving Toward an Integrated, Holistic Analytical Response. Journal of Analytical Toxicology. 2019;43:1-9.
- ²⁸² Levine M, Sanko S, Eckstein M. Assessing the Risk of Prehospital Administration of Naloxone with Subsequent Refusal of Care. Prehospital Emergency Care. 2016;20:566-9.
- ²⁸³ Zachariah BS, Bryan D, Pepe PE, Griffin M. Follow-up and Outcome of Patients Who Decline or are Denied Transport by EMS. Prehospital and Disaster Medicine. 1992;7:359-64.
- ²⁸⁴ Larochelle MR, Bernson D, Land T, Stopka TJ, Wang N, Xuan Z, Bagley SM, Liebschutz JM, Walley AY. Medication for Opioid Use Disorder After Nonfatal Opioid Overdose and Association with Mortality: A Cohort Study. Annals of Internal Medicine. 2018;169:137-45.
- ²⁸⁵ HELP4WV: West Virginia's Addiction & Mental Health Helpline. Annual Report – 2019. Available at: <https://static1.squarespace.com/static/59b197d98dd0417b88f2355f/t/5e3d9693575e635016abc533/1581094580746/HELP4WV+Annual+Report+2019.pdf>. Accessed May 4, 2020.
- ²⁸⁶ Mullins, C. A Public Health Emergency: West Virginia's Efforts to Curb the Opioid Crisis (Testimony). Published 2020. Available at: <https://docs.house.gov/meetings/IF/IF02/20200114/110367/HHRG-116-IF02-Wstate-MullinsC-20200114.pdf>. Accessed May 9, 2020.
- ²⁸⁷ HELP4WV: West Virginia's Addiction & Mental Health Helpline. Annual Report – 2019. Available at: <https://static1.squarespace.com/static/59b197d98dd0417b88f2355f/t/5e3d9693575e635016abc533/1581094580746/HELP4WV+Annual+Report+2019.pdf>. Accessed May 4, 2020.
- ²⁸⁸ Watson DP, Brucker K, McGuire A, Snow-Hill NL, Xu H, Cohen A, Campbell M, Robison L, Sights E, Buhner R, O'Donnell D, Kline JA. Replication of an Emergency Department-Based Recovery Coaching Intervention and Pilot Testing of Pragmatic Trial Protocols within the Context of Indiana's Opioid State Targeted Response Plan. J Subst Abuse Treat. 2020;108:88-94.
- ²⁸⁹ Samuels EA, Baird J, Yang ES, Mello MJ. Adoption and Utilization of an Emergency Department Naloxone Distribution and Peer Recovery Coach Consultation Program. Acad Emerg Med. 2019;26:160-73.
- ²⁹⁰ Substance Abuse and Mental Health Services Administration. Peers Supporting Recovery from Substance Use Disorders. Available at: https://www.samhsa.gov/sites/default/files/programs_campaigns/brss_tacs/peers-supporting-recovery-substance-use-disorders-2017.pdf. Accessed February 15, 2020.
- ²⁹¹ Reif S, Braude L, Lyman DR, Dougherty RH, Daniels AS, Ghose SS, Salim O, Delphin-Rittmon ME. Peer Recovery Support for Individuals with Substance Use Disorders: Assessing the Evidence. Psychiatric Services. 2014;65:853-61.

CONFIDENTIAL

-
- ²⁹² Bassuk EL, Hanson J, Greene RN, Richard M, Laudet A. Peer-Delivered Recovery Support Services for Addictions in the United States: A Systematic Review. *Journal of Substance Abuse Treatment*. 2016;63:1-9.
- ²⁹³ West Virginia Department of Health and Human Resources. Outbreak Report: Opioid-Related Overdose – Huntington, West Virginia. Published 2016. Available at: <https://oeps.wv.gov/outbreaks/documents/data/special/opioid-overdose-outbreak-report.pdf>. Accessed July 28, 2020.
- ²⁹⁴ D’Onofrio G, O’Connor PG, Pantalon MV, Chawarski MC, Busch SH, Owens PH, Bernstein SL, Fiellin DA. Emergency Department-Initiated Buprenorphine/Naloxone Treatment for Opioid Dependence: A Randomized Clinical Trial. *JAMA*. 2015;313:1636-44.
- ²⁹⁵ Regan S, Howard S, Powell E, Martin A, Dutta S, Hayes BD, White BA, Williamson D, Kehoe L, Raja AS, Wakeman SE. Emergency Department-Initiated Buprenorphine and Referral to Follow-up Addiction Care: A Program Description. *Journal of Addiction Medicine*. 2021.
- ²⁹⁶ Bogan C, Jennings L, Haynes L, Barth K, Moreland A, Oros M, Goldsby S, Lane S, Funcell C, Brady K. Implementation of Emergency Department-Initiated Buprenorphine for Opioid Use Disorder in a Rural Southern State. *Journal of Substance Abuse Treatment*. 2020;112:73-8.
- ²⁹⁷ Thomas CP, Stewart MT, Tschampl C, Sennaar K, Schwartz D, Dey J. Emergency Department Interventions for Opioid Use Disorder: A Synthesis of Emerging Models. *Journal of Substance Abuse Treatment*. 2022:108837.
- ²⁹⁸ University of California San Francisco. Addiction Care Team. Available at: <https://act.ucsf.edu/about>. Accessed June 21, 2021.
- ²⁹⁹ University of California San Francisco. Addiction Care Team. Available at: <https://act.ucsf.edu/about>. Accessed June 21, 2021.
- ³⁰⁰ Warren O, Smith-Bernardin S, Jamieson K, Zaller N, Liferidge A. Identification and Practice Patterns of Sobering Centers in the United States. *Journal of Health Care for the Poor and Underserved*. 2016;27:1843-57.
- ³⁰¹ Marshall B, McGlynn E, King A. Sobering Centers, Emergency Medical Services, and Emergency Departments: A Review of the Literature. *The American Journal of Emergency Medicine*, 2020.
- ³⁰² Smith-Bernardin S, Schneidermann M. Safe Sobering: San Francisco’s Approach to Chronic Public Inebriation. *Journal of Health Care for the Poor and Underserved*. 2012;23:265-70.
- ³⁰³ Smith-Bernardin SM, Kennel M, Yeh C. EMS Can Safely Transport Intoxicated Patients to a Sobering Center as an Alternate Destination. *Annals of Emergency Medicine*. 2019;74:112-8.
- ³⁰⁴ San Francisco Department of Public Health. Drug Sobering Center Issue Brief. Published 2021. Available at: https://www.sfdph.org/dph/files/IWG/Drug_Sobering_Center_Issue_Brief_FINAL.pdf. Accessed March 9, 2022.
- ³⁰⁵ Champagne-Langabeer T, Bakos-Block C, Yatsco A, Langabeer JR. Emergency Medical Services Targeting Opioid Use Disorder: An Exploration of Current Out-Of-Hospital Post-Overdose Interventions. *Journal of the American College of Emergency Physicians Open*. 2020;1:1230-9.
- ³⁰⁶ San Francisco Department of Public Health. Street Crisis Response Team (SCRT). Published 2021. Available at: https://www.sfdph.org/dph/files/IWG/SCRT_IWG_Issue_Brief_FINAL.pdf. Accessed June 15, 2021.
- ³⁰⁷ California Health Care Foundation. Overview: Community Paramedicine. Published April 2018. Available at: <https://www.chcf.org/wp-content/uploads/2018/05/CommunityParamedicinePilotProjects.pdf>. Accessed September 17, 2021.
- ³⁰⁸ Los Angeles Police Department. Mental Evaluation Unit. Available at: http://www.lapdonline.org/detective_bureau/content_basic_view/51704. Accessed February 25, 2020.
- ³⁰⁹ Krawczyk N, Buresh M, Gordon MS, Blue TR, Fingerhood MI, Agus D. Expanding Low-Threshold Buprenorphine to Justice-Involved Individuals Through Mobile Treatment: Addressing a Critical Care Gap. *Journal of Subst Abuse Treatment*. 2019;103:1-8.
- ³¹⁰ Bureau of Justice Assistance (BJA) Comprehensive Opioid, Stimulant, and Substance Abuse Program (COSSAP). Mobile Treatment for Opioid Use Disorder: Examples From the Field – Part I. Available at:

CONFIDENTIAL

https://www.cossapresources.org/Content/Documents/Articles/RTI_Mobile_Treatment_for_OUD.pdf. Accessed March 9, 2022.

³¹¹ Bureau of Justice Assistance (BJA) Comprehensive Opioid, Stimulant, and Substance Abuse Program (COSSAP). Mobile Treatment for Opioid Use Disorder: Examples From the Field – Part II. Available at:

https://www.cossapresources.org/Content/Documents/Articles/RTI_Mobile_Treatment_for_OUD_Part_2.pdf. Accessed March 9, 2022.

³¹² University of Pennsylvania Perelman School of Medicine. Rapid Initiation of Drug Treatment Engagement. Available at: <https://www.med.upenn.edu/hiv/ride.html>. Accessed March 9, 2022.

³¹³ Bridges Healthcare. Mobile Addiction Treatment Team (MATT) Van. Available at:

<https://www.bridgesct.org/website/publish/services/index.php?MATT-s-Van-36>. Accessed March 9, 2022.

³¹⁴ University of Maryland School of Medicine. Eastern Shore Mobile Care Collaborative (ESMCC) Home. Available at: <https://www.medschool.umaryland.edu/esmcc/>. Accessed March 9, 2022.

³¹⁵ University of Maryland School of Medicine. Eastern Shore Mobile Care Collaborative (ESMCC) Home. Available at: <https://www.medschool.umaryland.edu/esmcc/>. Accessed March 9, 2022.

³¹⁶ Colorado Department of Human Services. Mobile Health Services. Available at: <https://cdhs.colorado.gov/mobile-health-services>. Accessed March 9, 2022.

³¹⁷ University of Maryland School of Medicine. Eastern Shore Mobile Care Collaborative (ESMCC) Home. Available at: <https://www.medschool.umaryland.edu/esmcc/>. Accessed March 9, 2022.

³¹⁸ Weintraub E, Seneviratne C, Anane J, Coble K, Magidson J, Kattakuzhy S, Greenblatt A, Welsh C, Pappas A, Ross TL, Belcher AM. Mobile Telemedicine for Buprenorphine Treatment in Rural Populations with Opioid Use Disorder. JAMA Network Open. 2021;4:e2118487.

³¹⁹ Colorado Department of Human Services. Mobile Health Services. Available at: <https://cdhs.colorado.gov/mobile-health-services>. Accessed March 9, 2022.

³²⁰ Colorado Department of Human Services. Mobile Health Services. Available at: <https://cdhs.colorado.gov/mobile-health-services>. Accessed March 9, 2022.

³²¹ The Evaluation Center, University of Colorado Denver. State Opioid Response Grant: Mobile Health Units Delivering MAT Treatment Year Two Evaluation Report. Published 2020. Available at:

https://drive.google.com/file/d/18ATZ3FSoRrMNJfuh8qfc_Gbg-EhX1hy/view. Accessed March 9, 2022.

³²² The Evaluation Center, University of Colorado Denver. State Opioid Response Grant: Mobile Health Units Delivering MAT Treatment Year Two Evaluation Report. Published 2020. Available at:

https://drive.google.com/file/d/18ATZ3FSoRrMNJfuh8qfc_Gbg-EhX1hy/view. Accessed March 9, 2022.

³²³ United States Department of Agriculture. Rural America at a Glance. Economic Research Service (ERA) Economic Information Bulletin Number 230. Published 2021. Available at: <https://www.ers.usda.gov/webdocs/publications/102576/eib-230.pdf?v=4409#:~:text=The%2046%20million%20U.S.%20residents,23%2C000%20people%20compared%20with%20245%2C000>. Accessed July 25, 2022.

³²⁴ Lister JJ, Weaver A, Ellis JD, Himle JA, Ledgerwood DM. A Systematic Review of Rural-Specific Barriers to Medication Treatment for Opioid Use Disorder in the United States. American Journal of Drug and Alcohol Abuse. 2020;46:273-88.

³²⁵ Moran GE, Snyder CM, Noftsinger RF, Noda JK. Implementing Medication-Assisted Treatment for Opioid Use Disorder in Rural Primary Care: Environmental Scan, Volume 1. Agency for Healthcare Research and Quality. Published 2017. Available at: https://integrationacademy.ahrq.gov/sites/default/files/mat_for_oud_environmental_scan_volume_1_1.pdf. Accessed May 8, 2020.

³²⁶ Office of the Assistant Secretary for Planning and Evaluation, United States Department of Health and Human Services. Best Practices and Barriers to Engaging People with Substance Use Disorders in Treatment. Published 2019. Available at: <https://aspe.hhs.gov/system/files/pdf/260791/BestSUD.pdf>. Accessed May 9, 2020.

CONFIDENTIAL

-
- ³²⁷ National Institutes on Drug Abuse. Effective Treatments for Opioid Addiction. Published 2016. Available at: <https://www.drugabuse.gov/publications/effective-treatments-opioid-addiction/effective-treatments-opioid-addiction>. Accessed February 10, 2020.
- ³²⁸ Mauro PM, Gutkind S, Annunziato EM, Samples H. Use of Medication for Opioid Use Disorder Among US Adolescents and Adults With Need for Opioid Treatment, 2019. JAMA network open. 2022;5:e223821-.
- ³²⁹ American Society of Addiction Medicine. National Practice Guideline 2020, Focused Update. Available at: <https://www.asam.org/quality-care/clinical-guidelines/national-practice-guideline>.
- ³³⁰ Yarmolinsky A, Rettig RA. Federal Regulation of Methadone Treatment. National Academies Press, 1995.
- ³³¹ Jones CM, Compton WM, Han B, Baldwin G, Volkow ND. Methadone-Involved Overdose Deaths in the US Before and After Federal Policy Changes Expanding Take-Home Methadone Doses from Opioid Treatment Programs. JAMA Psychiatry. 2022.
- ³³² Substance Abuse and Mental Health Services Administration. Naltrexone. Updated 2022. Available at: <https://www.samhsa.gov/medication-assisted-treatment/treatment/naltrexone>. Accessed July 25, 2022.
- ³³³ Substance Abuse and Mental Health Services Administration. An Introduction to Extended-Release Injectable Naltrexone for the Treatment of People with Opioid Dependence. Published 2012. Available at: https://www.integration.samhsa.gov/Intro_To_Injectable_Naltrexone.pdf. Accessed February 10, 2020.
- ³³⁴ Drug Enforcement Administration. DEA Requirements for DATA Waived Physicians (DWP). Available at: <https://www.deadiversion.usdoj.gov/pubs/docs/index.html>. Accessed February 10, 2020.
- ³³⁵ Substance Abuse and Mental Health Services Administration. Buprenorphine. Published 2019. Available at: <https://www.samhsa.gov/medication-assisted-treatment/treatment/buprenorphine>. Accessed June 14, 2022.
- ³³⁶ Harper J. Price's Remarks on Opioid Treatment Were Unscientific and Damaging, Experts Say. National Public Radio. Published 2017. Available at: <https://www.npr.org/sections/health-shots/2017/05/16/528614422/prices-remarks-on-opioid-treatment-were-unscientific-and-damaging-experts-say>. Accessed February 10, 2020.
- ³³⁷ Volkow ND, Frieden TR, Hyde PS, Cha SS. Medication-Assisted Therapies - Tackling the Opioid-Overdose Epidemic. The New England Journal of Medicine. 2014;370:2063-6.
- ³³⁸ Mattick RP, Breen C, Kimber J, Davoli M. Methadone Maintenance Therapy Versus No Opioid Replacement Therapy for Opioid Dependence. Cochrane Database Syst Rev. 2009;CD002209.
- ³³⁹ Substance Abuse and Mental Health Services Administration. Medication and Counseling Treatment. Published 2020. Available at: <https://www.samhsa.gov/medication-assisted-treatment/treatment>. Accessed February 15, 2020.
- ³⁴⁰ World Health Organization Model List of Essential Medicines, 21st List. Geneva: World Health Organization. Published 2019. Available at: <https://apps.who.int/iris/bitstream/handle/10665/325771/WHO-MVP-EMP-IAU-2019.06-eng.pdf>. Accessed July 25, 2022.
- ³⁴¹ Saha TD, Kerridge BT, Goldstein RB, Chou SP, Zhang H, Jung J, Pickering RP, Ruan WJ, Smith SM, Huang B, Hasin DS. Nonmedical Prescription Opioid Use and DSM-5 Nonmedical Prescription Opioid Use Disorder in the United States. The Journal of Clinical Psychiatry. 2016;77:772-80.
- ³⁴² Knudsen HK, Roman PM, Oser CB. Facilitating Factors and Barriers to the Use of Medications in Publicly Funded Addiction Treatment Organizations. Journal of Addiction Medicine. 2010;4:99-107.
- ³⁴³ Substance Abuse and Mental Health Services Administration. National Survey of Substance Abuse Treatment Services (N-SSATS): 2016. Available at: https://www.samhsa.gov/data/sites/default/files/2016_NSSATS.pdf. Accessed February 15, 2020.
- ³⁴⁴ Sandoe E, Fry C, Frank R. Policy Levers That States Can Use to Improve Opioid Addiction Treatment and Address the Opioid Epidemic. Health Affairs Blog. Published 2018. Available at: <https://www.healthaffairs.org/doi/10.1377/hblog20180927.51221/full>. Accessed February 15, 2020.

CONFIDENTIAL

-
- ³⁴⁵ Timko C, Schultz NR, Cucciare MA, Vittorio L, Garrison-Diehn C. Retention in Medication-Assisted Treatment for Opiate Dependence: A Systematic Review. *Journal of Addictive Diseases*. 2016;35:22-35.
- ³⁴⁶ Daubresse M, Saloner B, Pollack HA, Alexander GC. Non-Buprenorphine Opioid Utilization Among Patients Using Buprenorphine. *Addiction*. 2017;112:1045-53.
- ³⁴⁷ Kurdyak P, Gomes T, Yao Z, Mamdani MM, Hellings C, Fischer B, Rehm J, Bayoumi AM, Juurlink DN. Use of Other Opioids During Methadone Therapy: A Population-Based Study. *Addiction*. 2012;107:776-80.
- ³⁴⁸ Larochelle MR, Bernson D, Land T, Stopka TJ, Wang N, Xuan Z, Bagley SM, Liebschutz JM, Walley AY. Medication for Opioid Use Disorder After Nonfatal Opioid Overdose and Association with Mortality: A Cohort Study. *Annals of Internal Medicine*. 2018;169:137-45.
- ³⁴⁹ Santo T, Clark B, Hickman M, Grebely J, Campbell G, Sordo L, Chen A, Tran LT, Bharat C, Padmanathan P, Cousins G. Association of Opioid Agonist Treatment with All-Cause Mortality and Specific Causes of Death Among People with Opioid Dependence: A Systematic Review and Meta-Analysis. *JAMA Psychiatry*. 2021;78:979-93.
- ³⁵⁰ Mojtabai R, Mauro C, Wall MM, Barry CL, Olfson M. Medication Treatment for Opioid Use Disorders in Substance Use Treatment Facilities. *Health Affairs*. 2019;38:14-23.
- ³⁵¹ Saloner B, Stoller K, Alexander GC. Moving Addiction Care to the Mainstream - Improving the Quality of Buprenorphine Treatment. *The New England Journal of Medicine*. 2018;379:4-6.
- ³⁵² Wakeman SE, Barnett ML. Primary Care and the Opioid-Overdose Crisis - Buprenorphine Myths and Realities. *The New England Journal of Medicine*. 2018;379:1-4.
- ³⁵³ Matusow H, Dickman SL, Rich JD, Fong C, Dumont DM, Hardin C, Marlowe D, Rosenblum A. Medication Assisted Treatment in U.S. Drug Courts: Results from a Nationwide Survey of Availability, Barriers and Attitudes. *Journal of Substance Abuse Treatment*. 2013;44:473-80.
- ³⁵⁴ Heyward J, Jones CM, Compton WM, Lin DH, Losby JL, Murimi IB, Baldwin GT, Ballreich JM, Thomas D, Bicket M, Porter L, Tierce JC, Alexander GC. Coverage of Nonpharmacologic Treatments for Low Back Pain Among U.S. Public and Private Insurers. *JAMA Network Open*. 2018;1:e183044.
- ³⁵⁵ Lin DH, Jones CM, Compton WM, Heyward J, Losby JL, Murimi IB, Baldwin GT, Ballreich JM, Thomas D, Bicket M, Porter L, Tierce JC, Alexander GC. Prescription Drug Coverage for Low Back Pain Among United States Medicaid, Medicare Advantage and Commercial Insurers. *JAMA Network Open*. 2018;1:e180235.
- ³⁵⁶ Peters R, Wengle E. Coverage of Substance-Use Disorder Treatments in Marketplace Plans in Six Cities. Urban Institute. Published 2016. Available at: <https://www.urban.org/sites/default/files/publication/81856/2000838-Coverage-of-Substance-Use-Disorder-Treatments-in-Marketplace-Plans-in-Six-Cities.pdf>. Accessed February 15, 2020.
- ³⁵⁷ United States Department of Defense, Office of the Secretary. TRICARE; Mental Health and Substance Use Disorder Treatment. Federal Register. Published 2016. Available at: <https://www.federalregister.gov/documents/2016/09/02/2016-21125/tricare-mental-health-and-substance-use-disorder-treatment>. Accessed February 15, 2020.
- ³⁵⁸ National Institute on Drug Abuse. How Much Does Opioid Treatment Cost?. Published 2018. Available at: <https://www.drugabuse.gov/publications/research-reports/medications-to-treat-opioid-addiction/how-much-does-opioid-treatment-cost>. Accessed February 15, 2020.
- ³⁵⁹ Eisenberg JM, Power EJ. Transforming Insurance Coverage Into Quality Health Care: Voltage Drops from Potential to Delivered Quality. *JAMA*. 2000;284:2100-7.
- ³⁶⁰ White W. Philadelphia Department of Behavioral Health and Intellectual Disability Services. Long-Term Strategies to Reduce the Stigma Attached to Addiction, Treatment, and Recovery within the City of Philadelphia (With Particular Reference to Medication-Assisted Treatment/Recovery). Published 2009. Available at: <https://dbhids.org/wp-content/uploads/2015/07/2009-Philadelphia-Papers-Long-Term-Strategies-to-Reduce-the-Stigma-Attached-to-Addiction.pdf>. Accessed February 15, 2020.
- ³⁶¹ Olsen Y, Sharfstein JM. Confronting the Stigma of Opioid Use Disorder – and its Treatment. *JAMA*. 2014;311:1393-4.

CONFIDENTIAL

-
- ³⁶² Centers for Disease Control and Prevention. Viral Hepatitis. Published 2018. Available at: <https://www.cdc.gov/hepatitis/statistics/index.htm>. Accessed February 15, 2020.
- ³⁶³ Han B, Compton WM, Blanco C, Crane E, Lee J, Jones CM. Prescription Opioid Use, Misuse and Use Disorders Among U.S. Adults: 2015 National Survey on Drug Use and Health. *Annals of Internal Medicine*. 2017;167:293-301.
- ³⁶⁴ Korthuis PT, McCarty D, Weimer M, Bougatsos C, Blazina I, Zakher B, Grusing S, Devine B, Chou R. Primary Care-Based Models for the Treatment of Opioid Use Disorder: A Scoping Review. *Annals of Internal Medicine*. 2017;166:268-78.
- ³⁶⁵ D'Onofrio G, O'Connor PG, Pantalon MV, Chawarski MC, Busch SH, Owens PH, Bernstein SL, Fiellin DA. Emergency Department-Initiated Buprenorphine/Naloxone Treatment for Opioid Dependence: A Randomized Clinical Trial. *JAMA*. 2015;313:1636-44.
- ³⁶⁶ Harris M, Johnson S, Mackin S, Saitz R, Walley AY, Taylor JL. Low Barrier Tele-Buprenorphine in the Time of COVID-19: A Case Report. *Journal of Addiction Medicine*. 2020;14:e136-8.
- ³⁶⁷ U.S. Drug Enforcement Agency. DEA SAMHSA Buprenorphine Telemedicine. Published 2020. Available at: [https://www.deadiversion.usdoj.gov/GDP/\(DEA-DC-022\)\(DEA068\)%20DEA%20SAMHSA%20buprenorphine%20telemedicine%20\(Final\)%20+Esign.pdf](https://www.deadiversion.usdoj.gov/GDP/(DEA-DC-022)(DEA068)%20DEA%20SAMHSA%20buprenorphine%20telemedicine%20(Final)%20+Esign.pdf). Accessed July 29, 2022.
- ³⁶⁸ Substance Abuse and Mental Health Services Administration. Statutes, Regulations, and Guidelines. Published 2022. Available at: <https://www.samhsa.gov/medication-assisted-treatment/statutes-regulations-guidelines>. Accessed July 29, 2022.
- ³⁶⁹ Substance Abuse and Mental Health Services Administration. Methadone Take-Home Flexibilities Extension Guidance. Published 2022. Available at: <https://www.samhsa.gov/medication-assisted-treatment/statutes-regulations-guidelines/methadone-guidance>. Accessed July 29, 2022.
- ³⁷⁰ Center for Substance Abuse Treatment. Substance Abuse: Clinical Issues in Intensive Outpatient Treatment, Treatment Improvement Protocol (TIP) Series, No. 47., Chapter 4. Services in Intensive Outpatient Treatment Programs. Published 2006. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK64094>. Accessed February 15, 2020.
- ³⁷¹ Friesen EL, Kurdyak P. The Impact of Psychiatric Comorbidity on Treatment Discontinuation Among Individuals Receiving Medications for Opioid Use Disorder. *Drug and Alcohol Dependence*. 2020;216:108244.
- ³⁷² Phillips SD, Burns BJ, Edgar ER, Mueser KT, Linkins KW, Rosenheck RA, Drake RE, McDonel Herr EC. Moving Assertive Community Treatment into Standard Practice. *Psychiatr Serv*. 2001;52:771-9.
- ³⁷³ Drake RE, McHugo GJ, Clark RE, Teague GB, Xie H, Miles K, Ackerson TH. Assertive Community Treatment for Patients with Co-occurring Severe Mental Illness and Substance Use Disorder: A Clinical Trial. *Am J Orthopsychiatry*. 1998;68:201-15.
- ³⁷⁴ Lehman AF, Dixon LB, Kernan E, DeForge BR, Postrado LT. A Randomized Trial of Assertive Community Treatment for Homeless Persons with Severe Mental Illness. *Archives of General Psychiatry*. 1997;54:1038-43.
- ³⁷⁵ Bond GR, Drake RE, Mueser KT, Latimer E. Assertive Community Treatment for People with Severe Mental Illness. *Disease Management and Health Outcomes*. 2001;9:141-59.
- ³⁷⁶ Clark RE, Teague GB, Ricketts SK, Bush PW, Xie H, McGuire TG, Drake RE, McHugo GJ, Keller AM, Zubkoff M. Cost-Effectiveness of Assertive Community Treatment Versus Standard Case Management for Persons With Co-Occurring Severe Mental Illness and Substance Use Disorders. *Health Serv Res*. 1998;33:1285-308.
- ³⁷⁷ Rosenheck RA, Neale MS. Cost-Effectiveness of Intensive Psychiatric Community Care for High Users of Inpatient Services. *Archives of General Psychiatry*. 1998;55:459-66.
- ³⁷⁸ Substance Abuse and Mental Health Services Administration. Assertive Community Treatment (ACT) Evidence-Based Practices (EBP) KIT. Published 2008. Available at: <https://store.samhsa.gov/product/Assertive-Community-Treatment-ACT-Evidence-Based-Practices-EBP-KIT/SMA08-4344>. Accessed June 15, 2020.
- ³⁷⁹ American Society of Addiction Medicine. The ASAM Criteria. Available at: <https://www.asam.org/resources/the-asam-criteria/about>. Accessed February 15, 2020.

CONFIDENTIAL

-
- ³⁸⁰ Alexander GC, Stoller KB, Haffajee RL, Saloner B. An Epidemic in the Midst of a Pandemic: Opioid Use Disorder and COVID-19. *Ann Intern Med.* 2020;173:57-8.
- ³⁸¹ National Institute of Drug Abuse. Misuse of Prescription Drugs. Published 2018. Available at: <https://www.drugabuse.gov/publications/misuse-prescription-drugs/overview>. Accessed February 15, 2020.
- ³⁸² Substance Abuse and Mental Health Services Administration. Key Substance Use and Mental Health Indicators in the United States: Results from the 2020 National Survey on Drug Use and Health. Published 2021. Available at: <https://www.samhsa.gov/data/sites/default/files/reports/rpt35325/NSDUHFFRPDFWHTMLFiles2020/2020NSDUHFFR1PDFW0102121.pdf>. Accessed June 13, 2022.
- ³⁸³ Substance Abuse and Mental Health Services Administration. Key Substance Use and Mental Health Indicators in the United States: Results from the 2019 National Survey on Drug Use and Health. Published 2020. Available at: <https://www.samhsa.gov/data/sites/default/files/reports/rpt29393/2019NSDUHFFRPDFWHTML/2019NSDUHFFR1PDFW090120.pdf>. Accessed June 13, 2022.
- ³⁸⁴ Substance Abuse and Mental Health Services Administration. Key Substance Use and Mental Health Indicators in the United States: Results from the 2020 National Survey on Drug Use and Health. Published 2021. Available at: <https://www.samhsa.gov/data/sites/default/files/reports/rpt35325/NSDUHFFRPDFWHTMLFiles2020/2020NSDUHFFR1PDFW0102121.pdf>. Accessed June 13, 2022.
- ³⁸⁵ Han B, Compton WM, Blanco C, Crane E, Lee J, Jones CM. Prescription Opioid Use, Misuse and Use Disorders in U.S. Adults: 2015 National Survey on Drug Use and Health. *Annals of Internal Medicine.* 2017;167:293-301.
- ³⁸⁶ Center for Disease Control and Prevention. U.S. Opioid Dispensing Rate Map. Available at: <https://www.cdc.gov/drugoverdose/maps/rxrate-maps.html>. Accessed April 27, 2021.
- ³⁸⁷ Substance Abuse and Mental Health Services Administration. National Survey on Drug Use and Health (NSDUH). Available at: <https://www.datafiles.samhsa.gov/>. Accessed April 27, 2021.
- ³⁸⁸ Johnson LD, Miech RA, O'Malley PM, Bachman JG, Schulenberg JE, Patrick ME. Monitoring the Future National Survey Results on Drug Use, 1975-2020: Overview, Key Findings on Adolescent Drug Use. Published 2021. Available at: <http://www.monitoringthefuture.org/pubs/monographs/mtf-overview2020.pdf>. Accessed April 27, 2021.
- ³⁸⁹ Han B, Compton WM, Blanco C, Crane E, Lee J, Jones CM. Prescription Opioid Use, Misuse, and Use Disorders in U.S. Adults: 2015 National Survey on Drug Use and Health. *Ann Intern Med.* 2017;167:293-301.
- ³⁹⁰ Ford JA, Pomykacz C, Szalewski A, McCabe SE, Schepis TS. Friends and Relatives as Sources of Prescription Opioids for Misuse Among Young Adults: The Significance of Physician Source and Race/Ethnic Differences. *Subst Abus.* 2020;41:93-100.
- ³⁹¹ Substance Abuse and Mental Health Services Administration. Key Substance Use and Mental Health Indicators in the United States: Results from the 2019 National Survey on Drug Use and Health. Published 2020. Available at: <https://www.samhsa.gov/data/sites/default/files/reports/rpt29393/2019NSDUHFFRPDFWHTML/2019NSDUHFFR1PDFW090120.pdf>. Accessed April 27, 2021.
- ³⁹² Substance Abuse and Mental Health Services Administration. Key Substance Use and Mental Health Indicators in the United States: Results from the 2019 National Survey on Drug Use and Health. Published 2020. Available at: <https://www.samhsa.gov/data/sites/default/files/reports/rpt29393/2019NSDUHFFRPDFWHTML/2019NSDUHFFR1PDFW090120.pdf>. Accessed April 27, 2021.
- ³⁹³ Substance Abuse and Mental Health Services Administration. Key Substance Use and Mental Health Indicators in the United States: Results from the 2019 National Survey on Drug Use and Health. Published 2020. Available at: <https://www.samhsa.gov/data/sites/default/files/reports/rpt29393/2019NSDUHFFRPDFWHTML/2019NSDUHFFR1PDFW090120.pdf>. Accessed April 27, 2021.
- ³⁹⁴ Han B, Compton WM, Blanco C, Crane E, Lee J, Jones CM. Prescription Opioid Use, Misuse, and Use Disorders in U.S. Adults: 2015 National Survey on Drug Use and Health. *Ann Intern Med.* 2017;167:293-301.

CONFIDENTIAL

-
- ³⁹⁵ National Conference on State Legislation. Prescribing Policies: States Confront Opioid Overdose Epidemic. Published 2019. Available at: <http://www.ncsl.org/research/health/prescribing-policies-states-confront-opioid-overdose-epidemic.aspx>. Accessed February 15, 2020.
- ³⁹⁶ Barnett ML, Olenski AR, Jena AB. Opioid-Prescribing Patterns of Emergency Physicians and Risk of Long-Term Use. *New England Journal of Medicine*. 2017;376:663-73.
- ³⁹⁷ Shah A, Hayes CJ, Martin BC. Characteristics of Initial Prescription Episodes and Likelihood of Long-Term Opioid Use - United States, 2006-2015. *MMWR Morb Mortal Wkly Rep*. 2017;66:265-9.
- ³⁹⁸ Deyo RA, Hallvik SE, Hildebran C, Marino M, Dexter E, Irvine JM, O’Kane N, Van Otterloo J, Wright DA, Leichtling G, Millet LM. Association Between Initial Opioid Prescribing Patterns and Subsequent Long-Term Use Among Opioid-Naïve Patients: A Statewide Retrospective Cohort Study. *Journal of General Internal Medicine*. 2017;32:21-7.
- ³⁹⁹ Jones CM, Paulozzi LJ, Mack KA. Sources of Prescription Opioid Pain Relievers by Frequency of Past-Year Nonmedical Use: United States, 2008-2011. *JAMA Internal Medicine*. 2014;174:802-3.
- ⁴⁰⁰ Han B, Compton WM, Blanco C, Crane E, Lee J, Jones CM. Prescription Opioid Use, Misuse, and Use Disorders in U.S. Adults: 2015 National Survey on Drug Use and Health. *Ann Intern Med*. 2017;167:293-301.
- ⁴⁰¹ Neuman MD, Bateman BT, Wunsch H. Inappropriate Opioid Prescription After Surgery. *The Lancet*. 2019;393:1547-57.
- ⁴⁰² Wunsch H, Wijeyesundera DN, Passarella MA, Neuman MD. Opioids Prescribed After Low-Risk Surgical Procedures in the United States, 2004-2012. *JAMA*. 2016;315:1654-7.
- ⁴⁰³ Shah R, Kuo YF, Westra J, Lin YL, Raji MA. Opioid Use and Pain Control After Total Hip and Knee Arthroplasty in the US, 2014 to 2017. *JAMA Network Open*. 2020;3:e2011972.
- ⁴⁰⁴ Hah JM, Bateman BT, Ratliff J, Curtin C, Sun E. Chronic Opioid Use After Surgery: Implications for Perioperative Management in the Face of the Opioid Epidemic. *Anesthesia and Analgesia*. 2017;125:1733.
- ⁴⁰⁵ Neuman MD, Bateman BT, Wunsch H. Inappropriate Opioid Prescription After Surgery. *The Lancet*. 2019;393:1547-57.
- ⁴⁰⁶ Bicket MC, Long JJ, Pronovost PJ, Alexander GC, Wu CL. Prescription Opioid Analgesics Commonly Unused After Surgery: A Systematic Review. *JAMA Surgery*. 2017;152:1066-71.
- ⁴⁰⁷ Harris K, Curtis J, Larsen B, Calder S, Duffy K, Bowen G, Hadley M, Tristani-Firouzi P. Opioid Pain Medication Use After Dermatologic Surgery: A Prospective Observational Study of 212 Dermatologic Surgery Patients. *JAMA Dermatol*. 2013;149:317-21.
- ⁴⁰⁸ Bates C, Laciak R, Southwick A, Bishoff J. Overprescription of Postoperative Narcotics: A Look at Postoperative Pain Medication Delivery, Consumption and Disposal in Urological Practice. *J Urol*. 2011;185:551-5.
- ⁴⁰⁹ Bicket MC, White E, Pronovost PJ, Wu CL, Yaster M, Alexander GC. Opioid Oversupply After Joint and Spine Surgery: A Prospective Cohort Study. *Anesthesia and Analgesia*. 2019;128:358-64.
- ⁴¹⁰ Armstrong GL, Wasley A, Simard EP, McQuillan GM, Kuhnert WL, Alter MJ. The Prevalence of Hepatitis C Virus Infection in the United States, 1999 through 2002. *Annals of Internal Medicine*. 2005;144:705-14.
- ⁴¹¹ HIV.gov. United States Statistics. Published 2020. Available at: <https://www.hiv.gov/hiv-basics/overview/data-and-trends/statistics>. Accessed February 15, 2020.
- ⁴¹² United States Department of Health and Human Services. HIV and Opportunistic Infections, Coinfections, and Conditions. Published 2019. Available at: <https://aidsinfo.nih.gov/understanding-hiv-aids/fact-sheets/26/88/hiv-and-hepatitis-c>. Accessed February 15, 2020.
- ⁴¹³ Compton WM, Jones CM, Baldwin GT. Relationship Between Nonmedical Prescription-Opioid Use and Heroin Use. *The New England Journal of Medicine*. 2016;374:154-63.
- ⁴¹⁴ Centers for Disease Control and Prevention. Vital Signs: Newly Reported Acute and Chronic Hepatitis C Cases – United States, 2009–2018. Published 2020. Available at:

CONFIDENTIAL

[https://www.cdc.gov/mmwr/volumes/69/wr/mm6914a2.htm#:~:text=The%20annual%20rate%20of%20reported%20acute%20hepatitis%20C%20cases%20per,years%20\(2.6\)%20in%202018](https://www.cdc.gov/mmwr/volumes/69/wr/mm6914a2.htm#:~:text=The%20annual%20rate%20of%20reported%20acute%20hepatitis%20C%20cases%20per,years%20(2.6)%20in%202018). Accessed June 13, 2022.

- ⁴¹⁵ Zibbell JE, Iqbal K, Patel RC, Suryaprasad A, Sanders KJ, Moore-Moravian L, Serrecchia J, Blankenship S, Ward JW, Holtzman D. Increases In Hepatitis C Virus Infection Related to Injection Drug Use Among Persons Aged ≤ 30 Years – Kentucky, Tennessee, Virginia, and West Virginia, 2006–2012. *Morbidity and Mortality Weekly Report*. 2015;64:453.
- ⁴¹⁶ Bruneau J, Roy É, Arruda N, Zang G, Jutras-Aswad D. The Rising Prevalence of Prescription Opioid Injection and its Association With Hepatitis C Incidence Among Street-Drug Users. *Addiction*. 2012;107:1318-27.
- ⁴¹⁷ Havens JR, Lofwall MR, Frost SD, Oser CB, Leukefeld CG, Crosby RA. Individual and Network Factors Associated With Prevalent Hepatitis C Infection Among Rural Appalachian Injection Drug Users. *American Journal of Public Health*. 2013;103:e44-52.
- ⁴¹⁸ Janowicz DM. HIV Transmission and Injection Drug Use: Lessons from the Indiana Outbreak. *Topics in Antiviral Medicine*. 2016;24:90-2.
- ⁴¹⁹ Conrad C, Bradley HM, Broz D, Buddha S, Chapman EL, Galang RR, Hillman D, Hon J, Hoover KW, Patel MR, Perez A. Communities Outbreak of HIV Infection Linked to Injection Drug Use of Oxymorphone - Indiana, 2015. *Morbidity and Mortality Weekly Report*. 2015;64:443.
- ⁴²⁰ Cipriano LE, Zaric GS, Holodniy M, Bendavid E, Owens DK, Brandeau ML. Cost Effectiveness of Screening Strategies for Early Identification of HIV and HCV Infection in Injection Drug Users. *PLoS One*. 2012;7:e45176.
- ⁴²¹ Centers for Disease Control and Prevention. HIV Testing. Available at: <https://www.cdc.gov/hiv/testing/index.html>. Accessed February 15, 2020.
- ⁴²² Calderon Y, Cowan E, Schramm C, Stern S, Brusalis C, Iscoe M, Rahman S, Verma R, Leider J. HCV and HBV Testing Acceptability and Knowledge Among Urban Emergency Department Patients and Pharmacy Clients. *Preventive Medicine*. 2014;61:29-33.
- ⁴²³ Stopka TJ, Marshall C, Bluthenthal RN, Webb DS, Truax SR. HCV and HIV Counseling and Testing Integration in California: An Innovative Approach to Increase HIV Counseling and Testing Rates. *Public Health Reports*. 2007;122:68-73.
- ⁴²⁴ Centers for Disease Control and Prevention. Hepatitis C Questions and Answers for the Public. Published 2020. Available at: <https://www.cdc.gov/hepatitis/hcv/cfaq.htm#F1>. Accessed February 15, 2020.
- ⁴²⁵ Marinho RT, Vitor S, Velosa J. Benefits of Curing Hepatitis C Infection. *Journal of Gastrointestinal and Liver Diseases*. 2014;23:85-90.
- ⁴²⁶ Leidner AJ, Chesson HW, Xu F, Ward JW, Spradling PR, Holmberg SD. Cost-Effectiveness of Hepatitis C Treatment for Patients in Early Stages of Liver Disease. *Hepatology*. 2015;61:1860-9.
- ⁴²⁷ Chhatwal J, Kanwal F, Roberts MS, Dunn MA. Cost-Effectiveness and Budget Impact of Hepatitis C Virus Treatment With Sofosbuvir and Ledipasvir in the United States. *Annals of Internal Medicine*. 2015;162:397-406.
- ⁴²⁸ Cepeda JA, Thomas DL, Astemborski J, Rudolph JE, Gicquelais R, Kirk GD, Mehta SH. Impact of Hepatitis C Treatment Uptake on Cirrhosis and Mortality in Persons Who Inject Drugs: A Longitudinal, Community-Based Cohort Study. *Annals of Internal Medicine*. 2022.
- ⁴²⁹ Cepeda JA, Thomas DL, Astemborski J, Rudolph JE, Gicquelais R, Kirk GD, Mehta SH. Impact of Hepatitis C Treatment Uptake on Cirrhosis and Mortality in Persons Who Inject Drugs: A Longitudinal, Community-Based Cohort Study. *Annals of Internal Medicine*. 2022.
- ⁴³⁰ Kitahata MM, Gange SJ, Abraham AG, Merriman B, Saag MS, Justice AC, Hogg RS, Deeks SG, Eron JJ, Brooks JT, Rourke SB. Effect of Early Versus Deferred Antiretroviral Therapy for HIV on Survival. *The New England Journal of Medicine*. 2009;360:1815-26.
- ⁴³¹ Kalichman SC. Co-Occurrence of Treatment Nonadherence and Continued HIV Transmission Risk Behaviors: Implications for Positive Prevention Interventions. *Psychosomatic Medicine*. 2008;70:593-7.

CONFIDENTIAL

-
- ⁴³² Mathew J, Addai T, Anand A, Morrobel A, Maheshwari P, Freels S. Clinical Features, Site of Involvement, Bacteriologic Findings, and Outcome of Infective Endocarditis in Intravenous Drug Users. *Arch Intern Med.* 1995;155:1641-8.
- ⁴³³ Harvard Health Publishing. Endocarditis. Published 2019. Available at: https://www.health.harvard.edu/a_to_z/endocarditis-a-to-z. Accessed April 15, 2021.
- ⁴³⁴ Fleischauer AT, Ruhl L, Rhea S, Barnes E. Hospitalizations for Endocarditis and Associated Health Care Costs Among Persons with Diagnosed Drug Dependence - North Carolina, 2010-2015. *MMWR Morb Mortal Wkly Rep.* 2017;66:569-73.
- ⁴³⁵ Wurcel AG, Anderson JE, Chui KK, Skinner S, Knox TA, Snyderman DR, Stopka TJ. Increasing Infectious Endocarditis Admissions Among Young People Who Inject Drugs. *Open Forum Infect Dis.* 2016;3:ofw157.
- ⁴³⁶ Murdoch DR, Corey GR, Hoen B, Miró JM, Fowler VG Jr, Bayer AS, Karchmer AW, Olaison L, Pappas PA, Moreillon P, Chambers ST, Chu VH, Falcó V, Holland DJ, Jones P, Klein JL, Raymond NJ, Read KM, Tripodi MF, Utili R, Wang A, Woods CW, Cabell CH; International Collaboration on Endocarditis-Prospective Cohort Study (ICE-PCS) Investigators. Clinical Presentation, Etiology, and Outcome of Infective Endocarditis in the 21st Century: The International Collaboration on Endocarditis-Prospective Cohort Study. *Arch Intern Med.* 2009;169:463-73.
- ⁴³⁷ Prendergast BD. The Changing Face of Infective Endocarditis. *Heart.* 2006; 92:879-85.
- ⁴³⁸ Thuny F, Grisoli D, Collart F, Habib G, Raoult D. Management of Infective Endocarditis: Challenges and Perspectives. *Lancet.* 2012; 379:965-75.
- ⁴³⁹ Kadri AN, Wilner B, Hernandez AV, Nakhoul G, Chahine J, Griffin B, Pettersson G, Grimm R, Navia J, Gordon S, Kapadia SR. Geographic Trends, Patient Characteristics, and Outcomes of Infective Endocarditis Associated With Drug Abuse in the United States From 2002 to 2016. *Journal of the American Heart Association.* 2019;8:e012969.
- ⁴⁴⁰ Kim JB, Ejiofor JI, Yammine M, Ando M, Camuso JM, Youngster I, Nelson SB, Kim AY, Melnitchouk SI, Rawn JD, MacGillivray TE. Surgical Outcomes of Infective Endocarditis Among Intravenous Drug Users. *The Journal of Thoracic and Cardiovascular Surgery.* 2016;152:832-41.
- ⁴⁴¹ Yuan SM. Right-Sided Infective Endocarditis: Recent Epidemiologic Changes. *Int J Clin Exp Med.* 2014;7:199-218.
- ⁴⁴² Kadri AN, Wilner B, Hernandez AV, Nakhoul G, Chahine J, Griffin B, Pettersson G, Grimm R, Navia J, Gordon S, Kapadia SR. Geographic Trends, Patient Characteristics, and Outcomes of Infective Endocarditis Associated With Drug Abuse in the United States from 2002 to 2016. *Journal of the American Heart Association.* 2019;8:e012969.
- ⁴⁴³ Day S, Patel N, Maffett S. Infective Endocarditis Trends Amongst Intravenous Drug Users: An Examination of Practice Patterns in a Mid-Western Tertiary Care Center. *Journal of the American College of Cardiology.* 2019;73:21.
- ⁴⁴⁴ Napoli N. Opioid Use Associated With Dramatic Rise in Dangerous Heart Infection. Available at: <https://www.acc.org/about-acc/press-releases/2019/03/06/10/36/opioid-use-associated-with-dramatic-rise-in-dangerous-heart-infection>. Accessed December 5, 2020.
- ⁴⁴⁵ Day S, Patel N, Maffett S. Infective Endocarditis Trends Amongst Intravenous Drug Users: An Examination of Practice Patterns in a Mid-Western Tertiary Care Center. *Journal of the American College of Cardiology.* 2019;73:21.
- ⁴⁴⁶ Kimmel SD, Walley AY, Li Y, Linas BP, Lodi S, Bernson D, Weiss RD, Samet JH, Laroche MR. Association of Treatment with Medications for Opioid Use Disorder with Mortality After Hospitalization for Injection Drug Use-Associated Infective Endocarditis. *JAMA Network Open.* 2020;3:e2016228.
- ⁴⁴⁷ Wohl AR, Carlos JA, Tejero J, Dierst-Davies R, Daar ES, Khanlou H, Cadden J, Towner W, Frye D. Barriers and Unmet Need for Supportive Services for HIV Patients in Care in Los Angeles County, California. *AIDS Patient Care and STDs.* 2011;25:525-32.
- ⁴⁴⁸ Allyn PR, O'Malley SM, Ferguson J, Tseng CH, Chew KW, Bhattacharya D. Attitudes and Potential Barriers Towards Hepatitis C Treatment in Patients With and Without HIV Coinfection. *International Journal of STD & AIDS.* 2018;29:334-40.
- ⁴⁴⁹ Martin A, Kunzler N, Nakagawa J, Lee B, Wakeman S, Weiner S, Raja AS. Get Waivered: A Resident-Driven Campaign to Address the Opioid Overdose Crisis. *Annals of Emergency Medicine.* 2019;74:691-6.

CONFIDENTIAL

-
- ⁴⁵⁰ Removing The X-Waiver is One Small Step Toward Increasing Treatment of Opioid Use Disorder, but Great Leaps are Needed. Health Affairs. Published 2021. Available at: <https://www.healthaffairs.org/doi/10.1377/hblog20210419.311749/full/>. Accessed June 15, 2021.
- ⁴⁵¹ Division of Addiction Sciences, Marshall University Joan C. Edwards School of Medicine. Resiliency Plan. Available at: https://jcesom.marshall.edu/media/58477/2020_cabell-county-resiliency-plan_final.pdf. Accessed April 25, 2020.
- ⁴⁵² Sorrell TR, Weber M, Alvarez A, Beste N, Hollins U, Amura CR, Cook PF. From Policy to Practice: Pilot Program Increases Access to Medication for Opioid Use Disorder in Rural Colorado. *J Subst Abuse Treat*. 2020;114:108027.
- ⁴⁵³ Strathdee SA, Ricketts EP, Huettner S, Cornelius L, Bishai D, Havens JR, Beilenson P, Rapp C, Lloyd JJ, Latkin CA. Facilitating Entry into Drug Treatment Among Injection Drug Users Referred from a Needle Exchange Program: Results from a Community-Based Behavioral Intervention Trial. *Drug and Alcohol Dependence*. 2006;83:225-32.
- ⁴⁵⁴ Traub O. Hospital Care Team Members. Published 2018. Available at: <https://www.merckmanuals.com/home/special-subjects/hospital-care/hospital-care-team-members>. Accessed July 23, 2020.
- ⁴⁵⁵ Hser YI, Mooney LJ, Saxon AJ, Miotto K, Bell DS, Zhu Y, Liang D, Huang D. High Mortality Among Patients with Opioid Use Disorder in a Large Healthcare System. *Journal of Addiction Medicine*. 2017;11:315.
- ⁴⁵⁶ Degenhardt L, Whiteford HA, Ferrari AJ, Baxter AJ, Charlson FJ, Hall WD, Freedman G, Burstein R, Johns N, Engell RE, Flaxman A. Global Burden of Disease Attributable to Illicit Drug Use and Dependence: Findings from the Global Burden of Disease Study 2010. *The Lancet*. 2013;382:1564-74.
- ⁴⁵⁷ Walley AY, Alperen JK, Cheng DM, Botticelli M, Castro-Donlan C, Samet JH, Alford DP. Office-Based Management of Opioid Dependence with Buprenorphine: Clinical Practices and Barriers. *Journal of General Internal Medicine*. 2008;23:1393-8.
- ⁴⁵⁸ University of California San Francisco Primary Care Addiction Medicine Fellowship. Available at: <https://hividgm.ucsf.edu/fellowships/ucsf-primary-care-addiction-medicine-fellowship>. Accessed March 15, 2021.
- ⁴⁵⁹ DeRonne BM, Wong KR, Schultz E, Jones E, Krebs EE. Implementation of a Pharmacist Care Manager Model to Expand Availability of Medications for Opioid Use Disorder. *American Journal of Health-System Pharmacy*. 2021;78:354-9.
- ⁴⁶⁰ Dimitropoulos E, Bertucci S, Wong K. Integration of a Clinical Pharmacy Specialist into a Substance Use Disorder Intensive Outpatient Treatment Program to Improve Prescribing Rates of Alcohol Use Disorder Pharmacotherapy. *Substance Abuse*. 2018;39:190-2.
- ⁴⁶¹ Wells I. Medication-Assisted Treatment for Opioid Use Disorder (OUD): Solving the Puzzle with Clinical Pharmacist Providers. *Journal of Pharmacy Practice*. 2020;33:124.
- ⁴⁶² Genoa Health Care. New Site Opening in San Francisco, CA. Published 2020. Available at: <https://www.genoahealthcare.com/insights/pharmacy-openings/new-site-opening-in-san-francisco-ca/>. Accessed October 1, 2021.
- ⁴⁶³ Robinson R. County Coroners and Their Role in the Heart of the Opioid Epidemic. *Academic Forensic Pathology*. 2017;7:80-86.
- ⁴⁶⁴ Association of State and Territorial Health Officials. Forensic Pathologist Shortages: Context and Considerations for Public Health Agencies. Published 2019. Available at: <https://www.astho.org/globalassets/brief/forensic-pathologist-shortage-context-considerations.pdf>. Accessed August 1, 2022.
- ⁴⁶⁵ American Medical Association. Issue Brief: Nation's Drug-Related Overdose and Death Epidemic Continues to Worsen. Published 2022. Available at: <https://www.ama-assn.org/system/files/issue-brief-increases-in-opioid-related-overdose.pdf>. Accessed August 1, 2022.
- ⁴⁶⁶ Sandbrink F, Uppal R. The Time for Opioid Stewardship is Now. *Joint Commission Journal on Quality and Patient Safety*. 2019;45:1-2.
- ⁴⁶⁷ Pedersen CA, Schneider PJ, Ganio MC, Scheckelhoff DJ. ASHP National Survey of Pharmacy Practice in Hospital Settings: Monitoring and Patient Education-2018. *American Journal of Health-System Pharmacy*. 2019;76:1038-58.

CONFIDENTIAL

-
- ⁴⁶⁸ Burnett Jr HJ, Wahl K. The Compassion Fatigue and Resilience Connection: A Survey of Resilience, Compassion Fatigue, Burnout, and Compassion Satisfaction Among Trauma Responders. *International Journal of Emergency Mental Health and Human Resilience*. 2015;17:318-26.
- ⁴⁶⁹ Burnett Jr HJ, Wahl K. The Compassion Fatigue and Resilience Connection: A Survey of Resilience, Compassion Fatigue, Burnout, and Compassion Satisfaction Among Trauma Responders. *International Journal of Emergency Mental Health and Human Resilience*. 2015;17:318-26.
- ⁴⁷⁰ Compass Project. Available at: <https://compasshuntington.com/>. Accessed April 25, 2020.
- ⁴⁷¹ Awa WL, Plaumann M, Walter U. Burnout Prevention: A Review of Intervention Programs. *Patient Education and Counseling*. 2010;78:184-90.
- ⁴⁷² National Institute on Drug Abuse. Opioid Overdose Reversal with Naloxone (Narcan, Evzio). Published 2020. Available at: <https://www.drugabuse.gov/related-topics/opioid-overdose-reversal-naloxone-narcan-evzio>. Accessed February 15, 2020.
- ⁴⁷³ Kerr D, Kelly AM, Dietze P, Jolley D, Barger B. Randomized Controlled Trial Comparing the Effectiveness and Safety of Intranasal and Intramuscular Naloxone for the Treatment of Suspected Heroin Overdose. *Addiction*. 2009;104:2067-74.
- ⁴⁷⁴ Clark AK, Wilder CM, Winstanley EL. A Systematic Review of Communities Opioid Overdose Prevention and Naloxone Distribution Programs. *Journal of Addiction Medicine*. 2014;8:153-63.
- ⁴⁷⁵ Giglio RE, Li G, DiMaggio CJ. Effectiveness of Bystander Naloxone Administration and Overdose Education Programs: A Meta-Analysis. *Injury Epidemiology*. 2015;2:10.
- ⁴⁷⁶ McDonald R, Strang J. Are Take-Home Naloxone Programmes Effective? Systematic Review Utilizing Application of the Bradford Hill Criteria. *Addiction*. 2016;111:1177-87.
- ⁴⁷⁷ Tas B, Humphreys K, McDonald R, Strang J. Should We Worry That Take-Home Naloxone Availability May Increase Opioid Use?. *Addiction*. 2019;114:1723-5.
- ⁴⁷⁸ Frank RG, Humphreys K, Pollack HA. Does Naloxone Availability Increase Opioid Abuse? The Case for Skepticism. *Health Affairs Blog*. Published 2018. Available at: <https://www.healthaffairs.org/doi/10.1377/hblog20180316.599095/full/>. Accessed February 15, 2020.
- ⁴⁷⁹ Ranapurwala SI, Shanahan ME, Alexandridis AA, Proescholdbell SK, Naumann RB, Edwards Jr D, Marshall SW. Opioid Overdose Mortality Among Former North Carolina Inmates: 2000–2015. *American Journal of Public Health*. 2018;108:1207-13.
- ⁴⁸⁰ Walley AY, Xuan Z, Hackman HH, Quinn E, Doe-Simkins M, Sorensen-Alawad A, Ruiz S, Ozonoff A. Opioid Overdose Rates and Implementation of Overdose Education and Nasal Naloxone Distribution in Massachusetts: Interrupted Time Series Analysis. *BMJ*. 2013;346:f174.
- ⁴⁸¹ Abouk R, Pacula RL, Powell D. Association Between State Laws Facilitating Pharmacy Distribution of Naloxone and Risk of Fatal Overdose. *JAMA Internal Medicine*. 2019;179:805-11.
- ⁴⁸² Capraro GA, Rebola CB. The NaloxBox Program in Rhode Island: A Model for Community-Access Naloxone. *American Journal of Public Health*. 2018;108:1649-51.
- ⁴⁸³ Substance Abuse and Mental Health Services Administration. Now What? The Role of Prevention Following a Nonfatal Opioid Overdose. Published 2018. Available at: https://www.edc.org/sites/default/files/uploads/role_of_prevention_following_and_overdose-v02.pdf. Accessed January 9, 2020.
- ⁴⁸⁴ Compton MT, Esterberg ML, McGee R, Kotwicki RJ, and Oliva JR. Crisis Intervention Team Training: Changes in Knowledge, Attitudes, and Stigma Related to Schizophrenia. *Psychiatric Services*. 2006;57:1199-202.
- ⁴⁸⁵ Demir B, Broussard B, Goulding SM, and Compton MT. Beliefs About Causes of Schizophrenia Among Police Officers Before and After Crisis Intervention Team Training. *Communities Mental Health Journal*. 2009;45:385-92.
- ⁴⁸⁶ Livingston JD, Milne T, Fang ML, Amari E. The Effectiveness of Interventions for Reducing Stigma Related to Substance Use Disorders: A Systematic Review. *Addiction*. 2012;107:39-50.

CONFIDENTIAL

-
- ⁴⁸⁷ Bahora M, Hanafi S, Chien VH, Compton MT. Preliminary Evidence of Effects of Crisis Intervention Team Training on Self-Efficacy and Social Distance. *Administration and Policy in Mental Health and Mental Health Services Research*. 2008;35:159-67.
- ⁴⁸⁸ Watson AC, Fulambarker AJ. The Crisis Intervention Team Model of Police Response to Mental Health Crises: A Primer for Mental Health Practitioners. *Best Practices in Mental Health*. 2012;8:71.
- ⁴⁸⁹ Teller JL, Munetz MR, Gil KM, Ritter C. Crisis Intervention Team Training for Police Officers Responding to Mental Disturbance Calls. *Psychiatric Services*. 2006;57:232-7.
- ⁴⁹⁰ Compton MT, Bakeman R, Broussard B, Hankerson-Dyson D, Husbands L, Krishan S, Stewart-Hutto T, D'Orio BM, Oliva JR, Thompson NJ, Watson AC. The Police-Based Crisis Intervention Team (CIT) Model: I. Effects on Officers' Knowledge, Attitudes, and Skills. *Psychiatric Services*. 2014;65:517-22.
- ⁴⁹¹ Law Enforcement Assisted Diversion (LEAD) National Support Bureau. Available at: <https://www.leadbureau.org>. Accessed February 15, 2020.
- ⁴⁹² National Institute of Justice. Program Profile: Law Enforcement Assisted Diversion (LEAD) Program, Seattle, Washington. Published 2016. Available at: <https://www.crimesolutions.gov/ProgramDetails.aspx?ID=477>. Accessed February 15, 2020.
- ⁴⁹³ Division of Addiction Sciences, Marshall University Joan C. Edwards School of Medicine. City of Solutions. Available at: <http://philanthropywv.org/content/uploads/2019/11/COS-Guidebook-Finalized-as-of-9-26-19.pdf>. Accessed April 25, 2020.
- ⁴⁹⁴ Collins SE, Lonczak HS, Clifasefi SL. Seattle's Law Enforcement Assisted Diversion (LEAD): Program Effects on Recidivism Outcomes. *Evaluation and Program Planning*. 2017;64:49-56.
- ⁴⁹⁵ Clifasefi SL, Collins SE. LEAD Program Evaluation: Describing LEAD Cases Management in Participants' Own Words. Harm Reduction Research and Treatment Center, University of Washington. Published 2016. Available at: https://www.sfdph.org/dph/files/leadSF/Reports/Specific-Aim-4-FINAL_UW-LEAD-Evaluation-Qualitative-Report-11.1.16_updated.pdf. Accessed February 15, 2020.
- ⁴⁹⁶ Collins SE, Lonczak HS, Clifasefi SL. Seattle's Law Enforcement Assisted Diversion (LEAD): Program Effects on Criminal Justice and Legal System Utilization and Costs. *Journal of Experimental Criminology*. 2019;15:201-11.
- ⁴⁹⁷ Clifasefi SL, Lonczak HS, Collins SE. Seattle's Law Enforcement Assisted Diversion (LEAD) Program: Within-Subjects Changes on Housing, Employment, and Income/Benefits Outcomes and Associations with Recidivism. *Crime & Delinquency*. 2017;63:429-45.
- ⁴⁹⁸ Law Enforcement Assisted Diversion (LEAD) National Support Bureau. Available at: <https://www.leadbureau.org>. Accessed February 15, 2020.
- ⁴⁹⁹ West Virginia Department of Corrections and Rehabilitation. 2015 West Virginia Recidivism Report. Published 2019. Available at: <https://dcr.wv.gov/resources/Documents/publications/Recidivism%202015.pdf>. Accessed July 13, 2020.
- ⁵⁰⁰ Baltimore Police Department. Policy 801 – Overdose Response and Investigation Protocol. Published 2016. Available at: https://www.baltimorepolice.org/sites/default/files/Policies/801_Overdose_Response_And_Investigation_Protocol.pdf. Accessed February 15, 2020.
- ⁵⁰¹ Bureau of Justice Statistics. Special Report: Drug Use, Dependence, and Abuse Among State Prisoners and Jail Inmates, 2007-2009. Published 2017. Available at: https://www.bjs.gov/content/pub/pdf/dudaspi0709_sum.pdf. Accessed February 15, 2020.
- ⁵⁰² Bronson J, Stroop J, Zimmer S, Berzofsky M. Drug Use, Dependence, and Abuse Among State Prisoners and Jail Inmates, 2007-2009. Published 2017. Available at: <https://www.bjs.gov/content/pub/pdf/dudaspi0709.pdf>. Accessed March 17, 2019.
- ⁵⁰³ Boutwell AE, Nijhawan A, Zaller N, Rich JD. Arrested on Heroin: A National Opportunity. *Journal of Opioid Management*. 2007;3:328-32.

CONFIDENTIAL

-
- ⁵⁰⁴ Marlowe DB, Hardin CD, Fox CL. Painting the Current Picture: A National Report on Drug Courts and Other Problem-Solving Courts in the United States. National Drug Court Institute. Published 2016. Available at: <https://www.ndci.org/wp-content/uploads/2016/05/Painting-the-Current-Picture-2016.pdf>. Accessed July 25, 2022.
- ⁵⁰⁵ Christie C, Baker C, Cooper R, Kennedy PJ, Madras B, Bondi B. The President's Commission on Combating Drug Addiction and the Opioid Crisis. Published 2017. Available at: https://trumpwhitehouse.archives.gov/sites/whitehouse.gov/files/images/Final_Report_Draft_11-15-2017.pdf. Accessed January 17, 2020.
- ⁵⁰⁶ Huddleston W, Marlowe DB. Painting The Current Picture: A National Report Card on Drug Courts and Other Problem-Solving Court Programs in the United States Volume II, Number 1. National Drug Court Institute. Published 2011. Available at: <https://www.ndci.org/sites/default/files/nadcp/PCP%20Report%20FINAL.PDF>. Accessed July 25, 2022.
- ⁵⁰⁷ United States Department of Justice, Office of Justice Programs. Drug Courts. Published 2022. Available at: <https://www.ncjrs.gov/pdffiles1/nij/238527.pdf>. Accessed July 25, 2022.
- ⁵⁰⁸ Mitchell O, Wilson DB, Eggers A, MacKenzie DL. Assessing the Effectiveness of Drug Courts on Recidivism: A Meta-Analytic Review of Traditional and Non-Traditional Drug Courts. *Journal of Criminal Justice*. 2012;40:60-71.
- ⁵⁰⁹ Substance Abuse and Mental Health Services Administration. Substance Abuse Treatment for Adults in the Criminal Justice System. Published 2005. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK64130/>. Accessed June 15, 2021.
- ⁵¹⁰ Chandler RK, Fletcher BW, Volkow ND. Treating Drug Abuse and Addiction in the Criminal Justice System: Improving Public Health and Safety. *JAMA*. 2009;301:183-90.
- ⁵¹¹ Williams, T. Opioid Users Are Filling Jails. Why Don't Jails Treat Them?. Published 2017. Available at: <https://www.nytimes.com/2017/08/04/us/heroin-addiction-jails-methadone-suboxone-treatment.html>. Accessed February 15, 2020.
- ⁵¹² Hedrich D, Alves P, Farrell M, Stover H, Moller L, Mayet S. The Effectiveness of Opioid Maintenance Treatment in Prison Settings: A Systematic Review. *Addiction*. 2012;107:501-17.
- ⁵¹³ Johns Hopkins Bloomberg School of Public Health. Medications for Opioid Use Disorder in Jails and Prisons: Moving Towards Universal Access. Published 2021. Available at: <https://americanhealth.jhu.edu/sites/default/files/2021-08/JHU-014%20OUD%20in%20Jail%20Report%20FINAL%20.pdf>. Accessed July 31, 2022.
- ⁵¹⁴ Santo T, Clark B, Hickman M, Grebely J, Campbell G, Sordo L, Chen A, Tran LT, Bharat C, Padmanathan P, Cousins G. Association of Opioid Agonist Treatment With All-Cause Mortality and Specific Causes of Death Among People With Opioid Dependence: A Systematic Review and Meta-Analysis. *JAMA Psychiatry*. 2021;78:979-93.
- ⁵¹⁵ Binswanger IA. Opioid Use Disorder and Incarceration-Hope for Ensuring the Continuity of Treatment. *The New England Journal of Medicine*. 2019;380:1193.
- ⁵¹⁶ Binswanger IA, Nowels C, Corsi KF, Long J, Booth RE, Kutner J, Steiner JF. From the Prison Door Right to the Sidewalk, Everything Went Downhill, A Qualitative Study of the Health Experiences of Recently Released Inmates. *International Journal of Law and Psychiatry*. 2011;34:249-55.
- ⁵¹⁷ Petersilia J. When Prisoners Come Home: Parole and Prisoner Reentry. Oxford University Press, 2003.
- ⁵¹⁸ Lattimore PK, Steffey DM, Visher CA. Prisoner Reentry in the First Decade of the Twenty-First Century. *Victims and Offenders*. 2010;5:253-67.
- ⁵¹⁹ The National Reentry Resource Center. Available at: <https://csgjusticecenter.org/nrrc>. Accessed February 25, 2020.
- ⁵²⁰ Hunter SB, Huang CY. Substance Use Treatment and Reentry (STAR) Program: Final Evaluation Report. RAND Health Quarterly. Published 2014. Available at: https://www.rand.org/pubs/research_reports/RR572.html. Accessed July 25, 2022.
- ⁵²¹ Scaggs S, Bales WD, Clark C, Ensley D, Coltharp P, Blomberg TG. An Assessment of Substance Abuse Treatment Programs in Florida's Prisons Using a Random Assignment Experimental Design. Published 2016. Available at: <https://www.ncjrs.gov/App/Publications/abstract.aspx?ID=272003>. Accessed February 15, 2020.

CONFIDENTIAL

-
- ⁵²² Council of State Governments Justice Center. Best Practices for Successful Reentry for People Who Have Opioid Addictions. Published 2018. Available at: <https://www.ncjrs.gov/App/Publications/abstract.aspx?ID=275202>. Accessed February 15, 2020.
- ⁵²³ Barnes M, Irvine A, Ortega N. Santa Clara County Adult Reentry Strategic Plan Ready to Change: Promoting Safety and Health for the Whole Communities. Published 2012. Available at: <https://www.sccgov.org/sites/reentry/governance/Documents/SCC-Reentry-Strategic-Plan-Board-Approved-10-23-2012.pdf>. Accessed February 25, 2020.
- ⁵²⁴ Baer D, Bhati A, Brooks L, Castro J, Vigne N, Mallik-Kane K, Naser R, Osborne J, Roman C, Roman J, Rossman S, Solomon A, Visser C, Winterfield L. Understanding the Challenges of Prisoner Reentry: Research Findings from the Urban Institute's Prisoner Reentry Portfolio. Urban Institute. Published 2006. Available at: <https://www.urban.org/sites/default/files/publication/42981/411289-Understanding-the-Challenges-of-Prisoner-Reentry.PDF>. Accessed June 15, 2021.
- ⁵²⁵ Prison Policy Initiative. Nowhere to Go: Homelessness Among Formerly Incarcerated People. Available at: <https://www.prisonpolicy.org/reports/housing.html>. Accessed June 15, 2021.
- ⁵²⁶ Walton MT, Hall MT. The Effects of Employment Interventions on Addiction Treatment Outcomes: A Review of the Literature. *Journal of Social Work Practice in the Addictions*. 2016;16:358-84.
- ⁵²⁷ Case A, Deaton A. *Deaths of Despair and the Future of Capitalism*. Princeton University Press, 2020.
- ⁵²⁸ Ruhm CJ. Deaths of Despair or Drug Problems? National Bureau of Economic Research. Published 2018. Available at: <https://www.nber.org/papers/w24188.pdf>. Accessed February 15, 2020.
- ⁵²⁹ Venkataramani AS, Bair EF, O'Brien RL, Tsai AC. Association Between Automotive Assembly Plant Closures and Opioid Overdose Mortality in the United States: A Difference-in-Differences Analysis. *JAMA Internal Medicine*. 2020;180:254-62.
- ⁵³⁰ Chatterji P, Meara E. Consequences of Eliminating Federal Disability Benefits for Substance Abusers. *J Health Econ*. 2010;29:226-40.
- ⁵³¹ Davies P, Iams H, Rupp K. The Effect of Welfare Reform on SSA's Disability Programs: Design of Policy Evaluation and Early Evidence. *Soc Secur Bull*. 2000;63:3-11.
- ⁵³² Hogan SR, Speigman R, Norris JC. The Effects of Eliminating Supplemental Security Income Drug Addiction and Alcoholism Eligibility on the Mental Health of Low-Income Substance Abusers. *Soc Work Public Health*. 2010;25:438-53.
- ⁵³³ Ellis MS, Kasper ZA, Cicero TJ. The Impact of Opioid Use Disorder on Levels of Educational Attainment: Perceived Benefits and Consequences. *Drug and Alcohol Dependence*. 2020;206:107618.
- ⁵³⁴ Richardson L, Wood E, Montaner J, Kerr T. Addiction Treatment-Related Employment Barriers: The Impact of Methadone Maintenance. *J Subst Abuse Treat*. 2012;43:276-84.
- ⁵³⁵ Center for Substance Abuse Treatment. Integrating Substance Abuse Treatment and Vocational Services. Treatment Improvement Protocol (TIP) Series 38. U.S. Department of Health and Human Services. Available at: <https://store.samhsa.gov/sites/default/files/d7/priv/sma12-4216.pdf>. Accessed July 25, 2022.
- ⁵³⁶ Shepard DS, Reif S. The Value of Vocational Rehabilitation in Substance User Treatment: A Cost-Effectiveness Framework. *Substance Use & Misuse*. 2004;39:2581-609.
- ⁵³⁷ Marsden J, Anders P, Clark H, et al. Protocol for a Multi-centre, Definitive Randomised Controlled Trial of the Effectiveness of Individual Placement and Support for Employment Support Among People with Alcohol and Drug Dependence. *Trials*. 2020;21:167.
- ⁵³⁸ Center for Substance Abuse Treatment. Integrating Substance Abuse Treatment and Vocational Services. Treatment Improvement Protocol (TIP) Series 38. U.S. Department of Health and Human Services. Available at: <https://store.samhsa.gov/sites/default/files/d7/priv/sma12-4216.pdf>. Accessed July 25, 2022.

CONFIDENTIAL

-
- ⁵³⁹ Schuman-Olivier Z, Sundaram S. Creating Recovery-Friendly Workplaces. Published 2018. Available at: <https://www.health.harvard.edu/blog/creating-recovery-friendly-workplaces-2018120615520>. Accessed April 15, 2021.
- ⁵⁴⁰ Appelbaum PS and Parks J. Holding Insurers Accountable for Parity in Coverage of Mental Health Treatment. *Psychiatric Services*. 2020;71:202-4.
- ⁵⁴¹ Center for Substance Abuse Treatment. Integrating Substance Abuse Treatment and Vocational Services. Treatment Improvement Protocol (TIP) Series 38. U.S. Department of Health and Human Services. Available at: <https://store.samhsa.gov/sites/default/files/d7/priv/sma12-4216.pdf>. Accessed July 25, 2022.
- ⁵⁴² Ompad DC, Gershon RR, Sandh S, Acosta P, Palamar JJ. Construction Trade and Extraction Workers: A Population at High Risk for Drug Use in the United States, 2005-2014. *Drug Alcohol Depend*. 2019;205:107640.
- ⁵⁴³ Rosenheck RA, Mares AS. Implementation of Supported Employment for Homeless Veterans with Psychiatric or Addiction Disorders: Two-Year Outcomes. *Psychiatr Serv*. 2007;58:325-33.
- ⁵⁴⁴ Frederick DE, VanderWeele TJ. Supported employment: Meta-Analysis and Review of Randomized Controlled Trials of Individual Placement and Support. *PLoS One*. 2019;14:e0212208.
- ⁵⁴⁵ Frederick DE, VanderWeele TJ. Supported employment: Meta-Analysis and Review of Randomized Controlled Trials of Individual Placement and Support. *PLoS One*. 2019;14:e0212208.
- ⁵⁴⁶ Gupta H. The Power of Fully Supporting Communities College Students: The Effects of The City University of New York's Accelerated Study in Associate Programs after Six Years. MDRC. Published 2017. Available at: <https://files.eric.ed.gov/fulltext/ED579083.pdf>. Accessed May 26, 2021.
- ⁵⁴⁷ Weiss MJ, Ratledge A, Sommo C, Gupta H. Supporting Communities College Students from Start to Degree Completion: Long-Term Evidence from a Randomized Trial of CUNY's ASAP. *American Economic Journal: Applied Economics*. 2019;11:253-97.
- ⁵⁴⁸ Miller C, Headlam C, Manno M, Cullinan D. Increasing Communities College Graduation Rates with a Proven Model: Three-Year Results from the Accelerated Study in Associate Programs (ASAP) Ohio Demonstration. MDRC. 2020.
- ⁵⁴⁹ Ban the Box Campaign. Available at: <http://bantheboxcampaign.org/about/#.YAdOisVufMI>. Accessed April 15, 2021.
- ⁵⁵⁰ Flake DF. Do Ban-the-Box Laws Really Work. *Iowa Law Review*. 2019;104:1079-127.
- ⁵⁵¹ Cook F, Halpin SM. Understanding Grief After an Overdose Death. National Network of Libraries of Medicine New England Region (NNLM NER) Repository. Published 2018. Available at: <https://doi.org/10.13028/rwre-cx49>. Accessed April 15, 2021.
- ⁵⁵² Feigelman W, Feigelman B, Range LM. Grief and Healing Trajectories of Drug-Death-Bereaved Parents. *Journal of Death and Dying*. 2020;80:629-47.
- ⁵⁵³ Feigelman W, Gorman BS, Jordan J. Parental Grief after a Child's Drug Death Compared to Other Death Causes: Investigating a Greatly Neglected Bereavement Problem Population. *Omega-Journal of Death and Dying*. 2011;63:291-316.
- ⁵⁵⁴ Children's Bureau. Parenting a Child Who Has Experienced Trauma. Published 2014. Available at: <https://www.childwelfare.gov/pubPDFs/child-trauma.pdf>. Accessed July 15, 2020.
- ⁵⁵⁵ Centers for Disease Control and Prevention. Children's Mental Health: Anxiety and Depression. Available at: <https://www.cdc.gov/childrensmentalhealth/depression.html>. Accessed July 15, 2020.
- ⁵⁵⁶ Felitti VJ, Anda RF, Nordenberg D, Williamson DF, Spitz AM, Edwards V, Marks JS. Relationship of Childhood Abuse and Household Dysfunction to Many of the Leading Causes of Death in Adults: The Adverse Childhood Experiences (ACE) Study. *American Journal of Preventive Medicine*. 1998;14:245-58.
- ⁵⁵⁷ Center for Disease Control and Prevention. About the CDC-Kaiser ACE Study. Available at: <https://www.cdc.gov/violenceprevention/aces/about.htmlhttps://www.cdc.gov/violenceprevention/acestudy/about.html>. Accessed April 15, 2021.

CONFIDENTIAL

-
- ⁵⁵⁸ Wolfson R. Working with UCSF, California Surgeon General Aims to Cut Adverse Childhood Experiences by Half. University of California San Francisco. Published 2020. Available at: <https://www.ucsf.edu/news/2020/02/416676/working-ucsf-california-surgeon-general-aims-cut-adverse-childhood-experiences>. Accessed June 15, 2021.
- ⁵⁵⁹ Young-Wolff KC, Sarovar V, Sterling SA, Leibowitz A, McCaw B, Hare CB, Silverberg MJ, Satre DD. Adverse Childhood Experiences, Mental Health, Substance Use, and HIV-Related Outcomes Among Persons with HIV. *AIDS Care*. 2019;31:1241-9.
- ⁵⁶⁰ West Virginia Department of Health and Human Resources. HSC Statistical Brief No. 30 Adverse Childhood Experiences. Published 2020. Available at: http://www.wvdhhr.org/bph/hsc/pubs/briefs/030/Brief30_Adverse_Childhood_Experiences.pdf. Accessed April 15, 2021.
- ⁵⁶¹ West Virginia Center for Children's Justice. Handle with Care. Available at: <http://www.handlewithcarewv.org/handle-with-care.php>. Accessed April 15, 2021.
- ⁵⁶² Health Resources & Services Administration. Health Professional Shortage Area (HPSA) Find Tool. Available at: <https://data.hrsa.gov/tools/shortage-area/hpsa-find>. Accessed April 15, 2021.
- ⁵⁶³ Hooten WM. Chronic Pain and Mental Health Disorders: Shared Neural Mechanisms, Epidemiology, and Treatment. *Mayo Clinic Proceedings*. 2016;91:955-70.
- ⁵⁶⁴ Carroll LJ, Cassidy JD, Côté P. Factors Associated with the Onset of an Episode of Depressive Symptoms in the General Population. *Journal of Clinical Epidemiology*. 2003;56:651-8.
- ⁵⁶⁵ Christidis P, Lin L, Stamm K. An Unmet Need for Mental Health Services. *Monitor on Psychology*. 2018;49:19.
- ⁵⁶⁶ Feigelman W, Feigelman B, Range LM. Grief and Healing Trajectories of Drug-Death-Bereaved Parents. *Journal of Death and Dying*. 2020;80:629-47.
- ⁵⁶⁷ Waugh A, Kiemle G, Slade P. What Aspects of Post-Traumatic Growth are Experienced by Bereaved Parents? A Systematic Review. *European Journal of Psychotraumatology*. 2018;9:1506230.
- ⁵⁶⁸ Cherkin DC, Sherman KJ, Balderson BH, Cook AJ, Anderson ML, Hawkes RJ, Hansen KE, Turner JA. Effect of Mindfulness-Based Stress Reduction vs Cognitive Behavioral Therapy or Usual Care on Back Pain and Functional Limitations in Adults with Chronic Low Back Pain: A Randomized Clinical Trial. *JAMA*. 2016;315:1240-9.
- ⁵⁶⁹ Åkerblom S, Perrin S, Fischer MR, McCracken LM. The Mediating Role of Acceptance in Multidisciplinary Cognitive-Behavioral Therapy for Chronic Pain. *The Journal of Pain*. 2015;16:606-15.
- ⁵⁷⁰ Foy JM, Green CM, Earls MF; Committee on Psychosocial Aspects of Child and Family Health, Mental Health Leadership Group. Mental Health Competencies for Pediatric Practice. *Pediatrics*. 2019;144:e20192757.
- ⁵⁷¹ Desai RJ, Hernandez-Diaz S, Bateman BT, Huybrechts KF. Increase in Prescription Opioid Use During Pregnancy Among Medicaid-Enrolled Women. *Obstetrics and Gynecology*. 2014;123:997.
- ⁵⁷² Bateman BT, Hernandez-Diaz S, Rathmell JP, Seeger JD, Doherty M, Fischer MA, Huybrechts KF. Patterns of Opioid Utilization in Pregnancy in a Large Cohort of Commercial Insurance Beneficiaries in the United States. *Anesthesiology*. 2014;120:1216-24.
- ⁵⁷³ Ko JY, D'Angelo DV, Haight SC, Morrow B, Cox S, Salvesen von Essen B, Strahan AE, Harrison L, Tevendale HD, Warner L, Kroelinger CD, Barfield WD. Vital Signs: Prescription Opioid Pain Reliever Use During Pregnancy - 34 U.S. Jurisdictions, 2019. *Morbidity and Mortality Weekly Report*. 2020;69:897-903.
- ⁵⁷⁴ Patrick SW, Davis MM, Lehmann CU, Cooper WO. Increasing Incidence and Geographic Distribution of Neonatal Abstinence Syndrome: United States 2009 to 2012. *Journal of Perinatology*. 2015;35:650.
- ⁵⁷⁵ Coyle MG, Brogly SB, Ahmed MS, Patrick SW, Jones HE. Neonatal Abstinence Syndrome. *Nature Reviews Disease Primers*. 2018;4:1-17.
- ⁵⁷⁶ Hirai AH, Ko JY, Owens PL, Stocks C, Patrick SW. Neonatal Abstinence Syndrome and Maternal Opioid-Related Diagnoses in the US, 2010-2017. *JAMA*. 2021;325:146-55.

CONFIDENTIAL

-
- ⁵⁷⁷ Hirai AH, Ko JY, Owens PL, Stocks C, Patrick SW. Neonatal Abstinence Syndrome and Maternal Opioid-Related Diagnoses in the US, 2010-2017. *JAMA*. 2021;325:146-55.
- ⁵⁷⁸ Substance Abuse and Mental Health Services Administration. Clinical Guidance for Treating Pregnant and Parenting Women with Opioid Use Disorder and Their Infants. Published 2018. Available at: <https://store.samhsa.gov/product/Clinical-Guidance-for-Treating-Pregnant-and-Parenting-Women-With-Opioid-Use-Disorder-and-Their-Infants/SMA18-5054>. Accessed July 26, 2022.
- ⁵⁷⁹ American College of Obstetricians and Gynecologists. ACOG Committee Opinion, Opioid Use and Opioid Use Disorder in Pregnancy. Published 2017. Available at: <https://www.acog.org/Clinical-Guidance-and-Publications/Committee-Opinions/Committee-on-Obstetric-Practice/Opioid-Use-and-Opioid-Use-Disorder-in-Pregnancy#6>. Accessed February 15, 2020.
- ⁵⁸⁰ Stulac S, Bair-Merritt M, Wachman EM, Augustyn M, Howard C, Madoor N, Costello E. Children and Families of the Opioid Epidemic: Under the Radar. *Current Problems in Pediatric and Adolescent Health Care*. 2019;49:100637.
- ⁵⁸¹ Parolin M, Simonelli A. Attachment Theory and Maternal Drug Addiction: The Contribution to Parenting Interventions. *Frontiers in Psychiatry*. 2016;7:152.
- ⁵⁸² Werner D, Young NK, Dennis K, Amatetti S. Family-Centered Treatment for Women with Substance Use Disorders: History, Key Elements and Challenges. Substance Abuse and Mental Health Services Administration. Published 2007. Available at: https://www.samhsa.gov/sites/default/files/family_treatment_paper508v.pdf. Accessed April 15, 2021.
- ⁵⁸³ American College of Obstetricians and Gynecologists. ACOG Committee Opinion, Opioid Use and Opioid Use Disorder in Pregnancy. Available at: <https://www.acog.org/Clinical-Guidance-and-Publications/Committee-Opinions/Committee-on-Obstetric-Practice/Opioid-Use-and-Opioid-Use-Disorder-in-Pregnancy#6>. Accessed March 9, 2019.
- ⁵⁸⁴ D'Onofrio G, O'Connor PG, Pantalon MV, Chawarski MC, Busch SH, Owens PH, Bernstein SL, Fiellin DA. Emergency Department-Initiated Buprenorphine/Naloxone Treatment for Opioid Dependence: A Randomized Clinical Trial. *JAMA*. 2015;313:1636-44.
- ⁵⁸⁵ BAART Programs. BAART Programs Market Street - San Francisco, California. Available at: <https://baartprograms.com/baart-market/>. Accessed September 9, 2021.
- ⁵⁸⁶ Coyle MG, Brogly SB, Ahmed MS, Patrick SW, Jones HE. Neonatal Abstinence Syndrome. *Nature Reviews Disease Primers*. 2018;4:1-17.
- ⁵⁸⁷ Nellhaus EM, Nieuwenhuizen L, Egletton R, Hansen Z, Chaffin D, Loudin S, Davies TH. History of Postpartum Depression as a Contributor to the Severity of NAS. *Addictive Behaviors*. 2019;89:78-84.
- ⁵⁸⁸ Werner D, Young NK, Dennis K, Amatetti S. Family-Centered Treatment for Women with Substance Use Disorders: History, Key Elements and Challenges. Substance Abuse and Mental Health Services Administration. Published 2007. Available at: https://www.samhsa.gov/sites/default/files/family_treatment_paper508v.pdf. Accessed April 15, 2021.
- ⁵⁸⁹ Substance Abuse and Mental Health Services Administration. Clinical Guidance for Treating Pregnant and Parenting Women with Opioid Use Disorder and Their Infants. Published 2018. Available at: <https://store.samhsa.gov/product/Clinical-Guidance-for-Treating-Pregnant-and-Parenting-Women-With-Opioid-Use-Disorder-and-Their-Infants/SMA18-5054>. Accessed July 26, 2022.
- ⁵⁹⁰ Substance Abuse and Mental Health Services Administration. National Survey on Drug Use and Health (NSDUH): 2019. Published 2022. Available at: <https://www.samhsa.gov/data/report/2020-nsduh-detailed-tables>. Accessed August 1, 2022.
- ⁵⁹¹ Comer S, Cunningham C, Fishman MJ, Gordon FA, Kampman FK, Langleben D, Nordstrom B, Oslin D, Woody G, Wright T, Wyatt S. National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use. *American Society of Addiction*. 2015;66.
- ⁵⁹² Office of Juvenile Justice and Delinquency Prevention. Consequences of Youth Substance Abuse. Published 1998. Available at: <https://www.ojjdp.gov/pubs/drugid/ration-03.html>. Accessed February 15, 2020.
- ⁵⁹³ Winters KC, Arria A. Adolescent Brain Development and Drugs. *The Prevention Researcher*. 2011;18:21.

CONFIDENTIAL

-
- ⁵⁹⁴ Blue Prints for Healthy Youth Development. Available at: <https://www.blueprintsprograms.org>. Accessed February 15, 2020.
- ⁵⁹⁵ Griffin KW, Botvin GJ. Evidence-Based Interventions for Preventing Substance Use Disorders in Adolescents. *Child and Adolescent Psychiatric Clinics*. 2010;19:505-26.
- ⁵⁹⁶ Strøm HK, Adolfsen F, Fossum S, Kaiser S, Martinussen M. Effectiveness of School-Based Preventive Interventions on Adolescent Alcohol Use: A Meta-Analysis of Randomized Controlled Trials. *Substance Abuse Treatment, Prevention, and Policy*. 2014;9:48.
- ⁵⁹⁷ Botvin Life Skills Training. Available at: <https://www.lifeskillstraining.com/fact-sheet>. Accessed February 15, 2020.
- ⁵⁹⁸ Spoth R, Trudeau L, Shin C, Ralston E, Redmond C, Greenberg M, Feinberg M. Longitudinal Effects of Universal Preventive Intervention on Prescription Drug Misuse: Three Randomized Controlled Trials with Late Adolescents and Young Adults. *American Journal of Public Health*. 2013;103:665-72.
- ⁵⁹⁹ Winters KC. Treatment of Adolescents with Substance Use Disorders: Treatment Improvement Protocol (TIP) Series 32. Substance Abuse and Mental Health Services Administration. Published 1999. Available at: <https://pa.performcare.org/assets/pdf/providers/quality-improvement/cpg/cpg-sud-tip-32-full.pdf>. Accessed February 15, 2020.
- ⁶⁰⁰ Bernstein SL, D'Onofrio G. Screening, Treatment Initiation, and Referral for Substance Use Disorders. *Addiction Science & Clinical Practice*. 2017;12:18.
- ⁶⁰¹ Bernstein SL, D'Onofrio G, Rosner J, O'Malley S, Makuch R, Busch S, Pantalon MV, Toll B. Successful Tobacco Dependence Treatment Achieved via Pharmacotherapy and Motivational Interviewing in Low-Income Emergency Department Patients. *Annals of Emergency Medicine*. 2015;66:140-7.
- ⁶⁰² D'Onofrio G, O'Connor PG, Pantalon MV, Chawarski MC, Busch SH, Owens PH, Bernstein SL, Fiellin DA. Emergency Department–Initiated Buprenorphine/Naloxone Treatment for Opioid Dependence: A Randomized Clinical Trial. *JAMA*. 2015;313:1636-44.
- ⁶⁰³ Kohomban J, Rodriguez J, Haskins R. The Foster Care System was Unprepared for the Last Drug Epidemic—Let's Not Repeat History. The Brookings Institute. Published 2018. Available at: <https://www.brookings.edu/blog/up-front/2018/01/31/the-foster-care-system-was-unprepared-for-the-last-drug-epidemic-lets-not-repeat-history>. Accessed February 15, 2020.
- ⁶⁰⁴ Kelly J. For Fifth Straight Year, U.S. Foster Care Totals Were Up in 2017. The Imprint. Published 2018. Available at: <https://imprintnews.org/child-welfare-2/for-fifth-straight-year-u-s-foster-care-totals-were-up-in-2017/32717>. Accessed July 26, 2022.
- ⁶⁰⁵ United States Department of Health and Human Services, Administration for Children and Families, Administration on Children, Youth and Families, Children's Bureau. 2020 AFCARS Report No. 28. Published 2021. Available at: <https://www.acf.hhs.gov/sites/default/files/documents/cb/afcarsreport28.pdf>. Accessed July 31, 2022.
- ⁶⁰⁶ United States Department of Health and Human Services, Administration for Children and Families, Administration on Children, Youth and Families, Children's Bureau. 2020 AFCARS Report No. 28. Published 2021. Available at: <https://www.acf.hhs.gov/sites/default/files/documents/cb/afcarsreport28.pdf>. Accessed July 31, 2022.
- ⁶⁰⁷ Young NK, Boles S, Otero C. Parental Substance Use Disorders and Child Maltreatment: Overlap, Gaps, and Opportunities. *Child Maltreatment*. 2007;12:137-49.
- ⁶⁰⁸ Seay K. How Many Families in Child Welfare Services are Affected by Parental Substance Use Disorders? A Common Question that Remains Unanswered. *Child Welfare*. 2015;94:19-51.
- ⁶⁰⁹ Wulczyn F, Ernst M, Fisher P. Who are the Infants in Out-of-Home Care? An Epidemiological and Developmental Snapshot. Chapin Hall Issue Brief. Published 2011. Available at: https://fcda.chapinhall.org/wp-content/uploads/2012/10/2011_infants_issue-brief.pdf. Accessed February 15, 2020.
- ⁶¹⁰ Lipari R, Van Horn SL. Children Living with Parents Who Have a Substance Use Disorder. Published 2017. Available at: https://www.samhsa.gov/data/sites/default/files/report_3223/ShortReport-3223.pdf. Accessed February 15, 2020.

CONFIDENTIAL

-
- ⁶¹¹ Clemans-Cope L, Lynch V, Epstein M, Kenney GM. Opioid and Substance Use Disorder and Receipt of Treatment Among Parents Living with Children in the United States, 2015-2017. *The Annals of Family Medicine*. 2019;17:207-11.
- ⁶¹² Wolf JP, Ponicki WR, Kepple NJ, Gaidus A. Are Community Level Prescription Opioid Overdoses Associated with Child Harm? A Spatial Analysis of California Zip Codes, 2001-2011. *Drug and Alcohol Dependence*. 2016;166:202-8.
- ⁶¹³ Radel L, Baldwin M, Crouse G, Ghertner R, Waters A. Substance Use, the Opioid Epidemic, and the Child Welfare System: Key Findings from a Mixed Methods Study. Published 2018. Available at: <https://aspe.hhs.gov/system/files/pdf/258836/SubstanceUseChildWelfareOverview.pdf>. Accessed February 15, 2020.
- ⁶¹⁴ Jee SH, Szilagyi M, Augustyn M. Comprehensive Health Care for Children in Foster Care. Published 2019. Available at: <https://www.uptodate.com/contents/comprehensive-health-care-for-children-in-foster-care>. Accessed February 15, 2020.
- ⁶¹⁵ North American Council on Adoptable Children. 2016 Saw More Children in Foster Care and More Adopted. Published 2016. Available at: <https://www.nacac.org/2018/01/08/2016-saw-more-children-in-foster-care-and-more-adopted>. Accessed February 15, 2020.
- ⁶¹⁶ Child Welfare Information Gateway. Parent-Child Interaction Therapy with At-Risk Families. Published 2013. Available at: https://www.childwelfare.gov/pubPDFs/f_interactbulletin.pdf. Accessed February 26, 2020.
- ⁶¹⁷ Child Welfare Information Gateway. Parent-Child Interaction Therapy with At-Risk Families. Published 2013. Available at: https://www.childwelfare.gov/pubPDFs/f_interactbulletin.pdf. Accessed February 26, 2020.
- ⁶¹⁸ Dahlhamer J, Lucas J, Zelaya C, Nahin R, Mackey S, DeBar L, Kerns R, Von Korff M, Porter L, Helmick C. Prevalence of Chronic Pain and High-Impact Chronic Pain Among Adults – United States, 2016. *Morbidity and Mortality Weekly Report*. 2018;67:1001-6.
- ⁶¹⁹ Zelaya CE, Dahlhamer JM, Lucas JW, Connor EM. Chronic Pain and High-Impact Chronic Pain Among U.S. Adults, 2019. *NCHS Data Brief*. 2020:1-8.
- ⁶²⁰ U.S. Department of Health and Human Services Office of Inspector General. Opioids in Medicare Part D: Concerns about Extreme Use and Questionable Prescribing. Published 2017. Available at: <https://oig.hhs.gov/oei/reports/oei-02-17-00250.pdf>. Accessed July 29, 2022.
- ⁶²¹ U.S. Department of Health and Human Services Office of Inspector General. Opioid Use Decreased in Medicare Part D, While Medication-Assisted Treatment Increased. Published 2019. Available at: <https://oig.hhs.gov/oei/reports/OEI-02-19-00390.pdf>. Accessed July 29, 2022.
- ⁶²² Moriya AS, Fang Z. Statistical Brief #541: Any Use and “Frequent Use” of Opioids Among Elderly Adults in 2018-2019, by Socioeconomic Characteristics. Published 2022. Available at: https://meps.ahrq.gov/data_files/publications/st541/stat541.shtml. Accessed July 29, 2022.
- ⁶²³ Kantor ED, Rehm CD, Haas JS, Chan AT, Giovannucci EL. Trends in Prescription Drug Use Among Adults in the United States from 1999-2012. *JAMA*. 2015;314:1818-30.
- ⁶²⁴ Ozenberger K, Alexander GC, Shin JI, Whitsel EA, Qato DM. Use of Prescription Medications With Cardiovascular Adverse Effects Among Older Adults in the United States. *Pharmacoepidemiology and Drug Safety*. 2022.
- ⁶²⁵ Weiner SG, El Ibrahimy S, Hendricks MA, Hallvik SE, Hildebran C, Fischer MA, Weiss RD, Boyer EW, Kreiner PW, Wright DA, Flores DP. Factors Associated with Opioid Overdose After an Initial Opioid Prescription. *JAMA Network Open*. 2022;5:e2145691.
- ⁶²⁶ Emeny RT, Chang CH, Skinner J, O'Malley AJ, Smith J, Chakraborti G, Rosen CJ, Morden NE. Association of Receiving Multiple, Concurrent Fracture-Associated Drugs with Hip Fracture Risk. *JAMA network open*. 2019;2:e1915348.
- ⁶²⁷ Maust DT, Strominger J, Kim HM, Langa KM, Bynum JP, Chang CH, Kales HC, Zivin K, Solway E, Marcus SC. Prevalence of Central Nervous System–Active Polypharmacy Among Older Adults with Dementia in the US. *JAMA*. 2021;325:952-961.
- ⁶²⁸ Rudd RA, Aleshire N, Zibbell JE, Gladden RM. Increases in Drug and Opioid Overdose Deaths – United States, 2000-2014. *MMWR Morbidity and Mortality Weekly Report*. 2016;64:1378-82.

CONFIDENTIAL

-
- ⁶²⁹ Mason M, Soliman R, Kim HS, Post LA. Disparities by Sex and Race and Ethnicity in Death Rates Due to Opioid Overdose Among Adults 55 Years or Older, 1999 to 2019. *JAMA Network Open*. 2022;5:e2142982.
- ⁶³⁰ Fingar KR, Owens PL. Statistical Brief #271: Opioid-Related and Stimulant-Related Adult Inpatient Stays, 2012–2018. Published 2021. Available at: <https://www.hcup-us.ahrq.gov/reports/statbriefs/sb271-Stimulant-Opioid-Hospitalizations-2012-2018.pdf>. Accessed July 29, 2022.
- ⁶³¹ U.S. Department of Health and Human Services Office of Inspector General. Medicare Part D Beneficiaries at Serious Risk of Opioid Misuse or Overdose: A Closer Look. Published 2020. Available at: <https://oig.hhs.gov/oei/reports/oei-02-19-00130.pdf>. Accessed July 29, 2022.
- ⁶³² U.S. Department of Health and Human Services Office of Inspector General. Concerns Persist About Opioid Overdoses and Medicare Beneficiaries' Access to Treatment and Overdose-Reversal Drugs. Published 2021. Available at: <https://oig.hhs.gov/oei/reports/OEI-02-20-00401.pdf>. Accessed July 29, 2022.
- ⁶³³ U.S. Department of Health and Human Services Office of Inspector General. Many Medicare Beneficiaries Are Not Receiving Medication to Treat Their Opioid Use Disorder. Published 2021. Available at: <https://oig.hhs.gov/oei/reports/OEI-02-20-00390.pdf>. Accessed July 29, 2022.
- ⁶³⁴ Courtwright DT. *Dark Paradise: A History of Opiate Addiction in America*. Harvard University Press. 1982.
- ⁶³⁵ Substance Abuse and Mental Health Services Administration. The Opioid Crisis and the Black/African American Population: An Urgent Issue. Published 2020. Available at: https://store.samhsa.gov/sites/default/files/SAMHSA_Digital_Download/PEP20-05-02-001_508%20Final.pdf. Accessed May 26, 2021.
- ⁶³⁶ Tipps RT, Buzzard GT, McDougall JA. The Opioid Epidemic in Indian Country. *The Journal of Law, Medicine & Ethics*. 2018;46:422-36.
- ⁶³⁷ Scholl L, Seth P, Kariisa M, Wilson N, Baldwin G. Drug and Opioid-Involved Overdose Deaths – United States, 2013–2017. *Morbidity and Mortality Weekly Report*. 2019;67:1419-27.
- ⁶³⁸ Scholl L, Seth P, Kariisa M, Wilson N, Baldwin G. Drug and Opioid-Involved Overdose Deaths – United States, 2013–2017. *Morbidity and Mortality Weekly Report*. 2019;67:1419-27.
- ⁶³⁹ Joshi S, Weiser T, Warren-Mears V. Drug, Opioid-Involved, and Heroin-Involved Overdose Deaths Among American Indians and Alaska Natives—Washington, 1999–2015. *Morbidity and Mortality Weekly Report*. 2018;67:1384-7.
- ⁶⁴⁰ Substance Abuse and Mental Health Services Administration (SAMHSA). 2019–2020 National Surveys on Drug Use and Health (NSDUH). Rockville, MD: Center for Behavioral Health Statistics and Quality. Available at: <https://www.samhsa.gov/data/sites/default/files/reports/rpt35323/NSDUHDetailedTabs2020/NSDUHDetailedTabs2020/NSDUHDetailedTabs2020.htm>. Accessed December 17, 2021.
- ⁶⁴¹ Kariisa M, Davis NL, Kumar S, et al. Vital Signs: Drug Overdose Deaths, by Selected Sociodemographic and Social Determinants of Health Characteristics – 25 States and the District of Columbia, 2019–2020. *MMWR Morb Mortal Wkly Rep*. 2022;71:940-7.
- ⁶⁴² Mason M, Soliman R, Kim HS, Post LA. Disparities by Sex and Race and Ethnicity in Death Rates Due to Opioid Overdose Among Adults 55 Years Or Older, 1999 to 2019. *JAMA Network Open*. 2022;5:e2142982.
- ⁶⁴³ Kariisa M, Davis NL, Kumar S, et al. Vital Signs: Drug Overdose Deaths, by Selected Sociodemographic and Social Determinants of Health Characteristics – 25 States and the District of Columbia, 2019–2020. *MMWR Morb Mortal Wkly Rep*. 2022;71:940-7.
- ⁶⁴⁴ Nelson A. Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care. *Journal of the National Medical Association*. 2002;94:666.
- ⁶⁴⁵ Daniel H, Bornstein SS, Kane GC. Addressing Social Determinants to Improve Patient Care and Promote Health Equity: An American College of Physicians Position Paper. *Ann Intern Med*. 2018;168:577-8.

CONFIDENTIAL

-
- ⁶⁴⁶ Meints SM, Cortes A, Morais CA, Edwards RR. Racial and Ethnic Differences in the Experience and Treatment of Noncancer Pain. *Pain Management*. 2019;9:317-34.
- ⁶⁴⁷ Mossey JM. Defining Racial and Ethnic Disparities in Pain Management. *Clinical Orthopaedics and Related Research*. 2011;469:1859-70.
- ⁶⁴⁸ Substance Abuse and Mental Health Services Administration (SAMHSA). The National Tribal Behavioral Health Agenda. <https://store.samhsa.gov/product/The-National-Tribal-Behavioral-Health-Agenda/PEP16-NTBH-AGENDA>. Accessed January 19, 2021.
- ⁶⁴⁹ United States Medicine. IHS Grapples with Pervasive Prescription Opioid Misuse in Tribal Areas. Published 2012. Available at: <http://www.usmedicine.com/clinical-topics/addiction/ihs-grapples-with-pervasive-prescription-opioid-misuse-in-tribal-areas>. Accessed January 19, 2021.
- ⁶⁵⁰ Substance Abuse and Mental Health Services Administration (SAMHSA). The National Tribal Behavioral Health Agenda. <https://store.samhsa.gov/product/The-National-Tribal-Behavioral-Health-Agenda/PEP16-NTBH-AGENDA>. Accessed January 19, 2021.
- ⁶⁵¹ Substance Abuse and Mental Health Services Administration (SAMHSA). The National Tribal Behavioral Health Agenda. <https://store.samhsa.gov/product/The-National-Tribal-Behavioral-Health-Agenda/PEP16-NTBH-AGENDA>. Accessed January 19, 2021.
- ⁶⁵² Substance Abuse and Mental Health Services Administration (SAMHSA). The National Tribal Behavioral Health Agenda. <https://store.samhsa.gov/product/The-National-Tribal-Behavioral-Health-Agenda/PEP16-NTBH-AGENDA>. Accessed January 19, 2021.
- ⁶⁵³ Mauro PM, Gutkind S, Annunziato EM, Samples H. Use of Medication for Opioid Use Disorder Among US Adolescents and Adults with Need for Opioid Treatment, 2019. *JAMA Network Open*. 2022;5:e223821.
- ⁶⁵⁴ Schiff DM, Nielsen T, Hoepfner BB, Terplan M, Hansen H, Bernson D, Diop H, Bharel M, Krans EE, Selk S, Kelly JF. Assessment of Racial and Ethnic Disparities in the Use of Medication to Treat Opioid Use Disorder Among Pregnant Women in Massachusetts. *JAMA Network Open*. 2020;3:e205734.
- ⁶⁵⁵ Substance Abuse and Mental Health Services Administration (SAMHSA). The Opioid Crisis and the Black/African American Population: An Urgent Issue. Published 2020. Available at: https://store.samhsa.gov/sites/default/files/SAMHSA_Digital_Download/PEP20-05-02-001_508%20Final.pdf. Accessed May 26, 2021.
- ⁶⁵⁶ Substance Abuse and Mental Health Services Administration (SAMHSA). The National Tribal Behavioral Health Agenda. <https://store.samhsa.gov/product/The-National-Tribal-Behavioral-Health-Agenda/PEP16-NTBH-AGENDA>. Accessed January 19, 2021.
- ⁶⁵⁷ Novins DK, Croy CD, Moore LA, Rieckmann T. Use of Evidence-Based Treatments in Substance Abuse Treatment Programs Serving American Indian and Alaska Native Communities. *Drug and Alcohol Dependence*. 2016;161:214-21.
- ⁶⁵⁸ Venner KL, Donovan DM, Campbell ANC, Wendt DC, Rieckmann T, Radin SM, Momper SL, Rosa CL. Future Directions for Medication Assisted Treatment for Opioid Use Disorder with American Indian/Alaska Natives. *Addictive Behaviors*. 2018;86:111-7.
- ⁶⁵⁹ Substance Abuse and Mental Health Services Administration (SAMHSA). The National Tribal Behavioral Health Agenda. <https://store.samhsa.gov/product/The-National-Tribal-Behavioral-Health-Agenda/PEP16-NTBH-AGENDA>. Accessed January 19, 2021.
- ⁶⁶⁰ American Civil Liberties Union. Cracks in the System: Twenty Years of the Unjust Federal Crack Cocaine Law. Published 2006. Available at: <https://www.aclu.org/other/cracks-system-20-years-unjust-federal-crack-cocaine-law>. Accessed June 15, 2021.
- ⁶⁶¹ Indian Health Services. Opioid Crisis Data: Understanding the Epidemic. Published 2018. Available at: <https://www.ihs.gov/opioids/opioidresponse/data/>. Accessed January 28, 2022.

CONFIDENTIAL

-
- ⁶⁶² Joshi S, Weiser T, Warren-Mears V. Drug, Opioid-Involved, and Heroin-Involved Overdose Deaths Among American Indians and Alaska Natives – Washington, 1999-2015. Morbidity and Mortality Weekly Report. 2018;67:1384-7.
- ⁶⁶³ Seven Directions: A Center for Indigenous Public Health. An Environmental Scan of Tribal Opioid Overdose Prevention Responses: Community-Based Strategies and Public Health Data Infrastructure. Published 2019. Available at: https://assets.website-files.com/5d68735d677c2aa989f0317b/5da8c57dcbe040a41d532331_ENV.SCAN_TribalOpioidOverdosePrevent_Sep2019-compressed.pdf. Accessed January 19, 2021.
- ⁶⁶⁴ Walters KL, Walls ML, Dillard DA, Kaur JS. American Indian and Alaska Native Research in the Health Sciences: Critical Considerations for the Review of Research Applications. Available at: https://dcpesi.nih.gov/sites/default/files/Critical_Considerations_for_Reviewing_AIAN_Research_508.pdf. Accessed December 16, 2021.
- ⁶⁶⁵ National Indian Health Board. Tribal Opioid Response Resource Toolkit. Available at: https://www.nihb.org/behavioral_health/tribal_opioid_response_resources.php. Accessed December 15, 2021.
- ⁶⁶⁶ National Congress of American Indians. NCAI Opioid Initiative. Available at: <https://www.ncai.org/initiatives/partnerships-initiatives/ncai-opioid-initiative>. Accessed December 15, 2021.
- ⁶⁶⁷ Indian County ECHO. Substance Use Disorder TeleECHO Program. Available at: <https://www.indiancountryecho.org/program/substance-use-disorder>. Accessed January 19, 2021.
- ⁶⁶⁸ Substance Abuse and Mental Health Services Administration (SAMHSA). The National Tribal Behavioral Health Agenda. <https://store.samhsa.gov/product/The-National-Tribal-Behavioral-Health-Agenda/PEP16-NTBH-AGENDA>. Accessed January 19, 2021.
- ⁶⁶⁹ United States Department of Housing and Urban Development. HUD Exchange. 2020 AHAR: Part 1 - PIT Estimates of Homelessness in the U.S. 2007 - 2020 Point-in-Time Estimates by CoC (XLSX). Available at: <https://www.hudexchange.info/resource/6291/2020-ahar-part-1-pit-estimates-of-homelessness-in-the-us/>. Accessed July 26, 2022.
- ⁶⁷⁰ Bucholtz S. Measuring Housing Insecurity in the American Housing Survey. Available at: <https://www.huduser.gov/portal/pdredge/pdr-edge-frm-asst-sec-111918.html>. Accessed April 15, 2021.
- ⁶⁷¹ United States Department of Housing and Urban Development. HUD 2019 Continuum of Care Homeless Assistance Programs Homeless Populations and Subpopulations. Published 2019. Available at: https://files.hudexchange.info/reports/published/CoC_PopSub_CoC_WV-501-2019_WV_2019.pdf. Accessed April 15, 2021.
- ⁶⁷² Tsai J, Kaspro WJ, Rosenheck RA. Latent Homeless Risk Profiles of a National Sample of Homeless Veterans and Their Relation to Program Referral and Admission Patterns. American Journal of Public Health. 2013;103:S239-47.
- ⁶⁷³ United States Conference of Mayors. Hunger and Homeless Survey: A Status Report on Hunger and Homelessness in America's Cities. Washington, DC: United States Conference of Mayors. Published 2014. Available at: <https://www2.cortland.edu/dotAsset/655b9350-995e-4aae-acd3-298325093c34.pdf>. Accessed July 26, 2022.
- ⁶⁷⁴ Hansen L, Penko J, Guzman D, Bangsberg DR, Miaskowski C, Kushel MB. Aberrant Behaviors with Prescription Opioids and Problem Drug Use History in a Communities-Based Cohort of HIV-Infected Individuals. Journal of Pain and Symptom Management. 2011;42:893-902.
- ⁶⁷⁵ United States Department of Health and Human Services, Office of the Assistant Secretary for Planning and Evaluation. Housing Options for Recovery for Individuals with Opioid Use Disorder: A Literature Review. Published 2019. Available at: <https://aspe.hhs.gov/system/files/pdf/261951/OUdlr.pdf>. Accessed February 15, 2020.
- ⁶⁷⁶ Baggett TP, Hwang SW, O'Connell JJ, Porneala BC, Stringfellow EJ, Orav EJ, Singer DE, Rigotti NA. Mortality Among Homeless Adults in Boston: Shifts in Causes of Death Over a 15-Year Period. JAMA Internal Medicine. 2013;173:189-95.
- ⁶⁷⁷ National Health Care for the Homeless Council. Fact Sheet: Addressing the Opioid Epidemic. Published 2017. Available at: <https://nhchc.org/wp-content/uploads/2019/08/nhchc-opioid-fact-sheet-august-2017.pdf>. Accessed February 15, 2020.

CONFIDENTIAL

-
- ⁶⁷⁸ Han BH, Doran KM, Krawczyk N. National Trends in Substance Use Treatment Admissions for Opioid Use Disorder Among Adults Experiencing Homelessness. *J Subst Abuse Treat.* 2022;132:108504.
- ⁶⁷⁹ Han BH, Doran KM, Krawczyk N. National Trends in Substance Use Treatment Admissions for Opioid Use Disorder Among Adults Experiencing Homelessness. *J Subst Abuse Treat.* 2022;132:108504.
- ⁶⁸⁰ Han BH, Doran KM, Krawczyk N. National Trends in Substance Use Treatment Admissions for Opioid Use Disorder Among Adults Experiencing Homelessness. *J Subst Abuse Treat.* 2022;132:108504.
- ⁶⁸¹ Rhoades H, Winetrobe H, Rice E. Prescription Drug Misuse Among Homeless Youth. *Drug and Alcohol Dependence.* 2014;138:229-33.
- ⁶⁸² United States Department of Health and Human Services, Office of the Assistant Secretary for Planning and Evaluation. Housing Options for Recovery for Individuals with Opioid Use Disorder: A Literature Review. Published 2019. Available at: <https://aspe.hhs.gov/system/files/pdf/261951/OUdlr.pdf>. Accessed February 15, 2020.
- ⁶⁸³ Gabrielian S, Young AS, Greenberg JM, Bromley E. Social Support and Housing Transitions Among Homeless Adults with Serious Mental Illness and Substance Use Disorders. *Psychiatric Rehabilitation Journal.* 2018;41:208.
- ⁶⁸⁴ United States Department of Health and Human Services, Office of the Assistant Secretary for Planning and Evaluation. Housing Options for Recovery for Individuals with Opioid Use Disorder: A Literature Review. Published 2019. Available at: <https://aspe.hhs.gov/system/files/pdf/261951/OUdlr.pdf>. Accessed February 15, 2020.
- ⁶⁸⁵ United States Department of Health and Human Services, Office of the Assistant Secretary for Planning and Evaluation. Housing Options for Recovery for Individuals with Opioid Use Disorder: A Literature Review. Published 2019. Available at: <https://aspe.hhs.gov/system/files/pdf/261951/OUdlr.pdf>. Accessed February 15, 2020.
- ⁶⁸⁶ Appel PW, Tsemberis S, Joseph H, Stefancic A, Lambert-Wacey D. Housing First for Severely Mentally Ill Homeless Methadone Patients. *Journal of Addictive Diseases.* 2012;31:270-7.
- ⁶⁸⁷ Ashwood, J. Scott, Karishma Patel, David Kravitz, David M. Adamson, and M. Audrey Burnam, Evaluation of the Homeless Multidisciplinary Street Team for the City of Santa Monica. Santa Monica, CA: RAND Corporation, 2019. Available at: https://www.rand.org/pubs/research_reports/RR2848.html. Accessed February 15, 2020.
- ⁶⁸⁸ United States Department of Housing and Urban Development. The 2019 Annual Homeless Report (AHAR) to Congress. Published 2020. Available at: <https://files.hudexchange.info/resources/documents/2019-AHAR-Part-1.pdf>. Accessed July 16, 2020.
- ⁶⁸⁹ National Association of Recovery Residences. NARR Levels of Recovery Support. Published 2016. Available at: https://narronline.org/wp-content/uploads/2016/12/NARR_levels_summary.pdf. Accessed February 15, 2020.
- ⁶⁹⁰ Thom K. Recovery Homes Help People in Early Recovery. Published 2016. Available at: <https://www.samhsa.gov/homelessness-programs-resources/hpr-resources/recovery-homes-help-people>. Accessed February 15, 2020.
- ⁶⁹¹ Reif S, George P, Braude L, Daugherty RH, Daniels AS, Ghose SS, Delphin-Rittmon AE. Recovery Housing: Assessing the Evidence. *Psychiatric Services.* 2014;65:295-300.
- ⁶⁹² United States Government Accountability Office. Substance Use Disorder: Information on Recovery Housing Prevalence, Selected States' Oversight, and Funding (GAO-18-315). Published 2018. Available at: <https://www.gao.gov/assets/700/690831.pdf>. Accessed February 15, 2020.
- ⁶⁹³ Han B, Compton WM, Blanco C, Crane E, Lee J, Jones CM. Prescription Opioid Use, Misuse, and Use Disorders in U.S. Adults: 2015 National Survey on Drug Use and Health. *Annals of Internal Medicine.* 2017;167:293-301.
- ⁶⁹⁴ Rosenblum A, Joseph H, Fong C, Kipnis S, Cleland C, Portenoy RK. Prevalence and Characteristics of Chronic Pain Among Chemically Dependent Patients in Methadone Maintenance and Residential Treatment Facilities. *JAMA.* 2003;289:2370-8.
- ⁶⁹⁵ Hser YI, Mooney LJ, Saxon AJ, Miotto K, Bell DS, Huang D. Chronic Pain Among Patients with Opioid Use Disorder: Results From Electronic Health Records Data. *Journal of Substance Abuse Treatment.* 2017;77:26-30.

CONFIDENTIAL

-
- ⁶⁹⁶ Dahlhamer J, Lucas J, Zelaya C, Nahin R, Mackey S, DeBar L, Kerns R, Von Korff M, Porter L, Helmick C. Prevalence of Chronic Pain and High-Impact Chronic Pain Among Adults – United States, 2016. *Morbidity and Mortality Weekly Report*. 2018;67:1001.
- ⁶⁹⁷ Agency for Healthcare Research and Quality. Noninvasive Nonpharmacological Treatment for Chronic Pain: A Systematic Review. Available at: <https://effectivehealthcare.ahrq.gov/sites/default/files/cer-209-evidence-summary-non-pharma-chronic-pain.pdf>. Accessed March 7, 2022.
- ⁶⁹⁸ McDonagh MS, Selph SS, Buckley DI, Holmes RS, Mauer K, Ramirez S, Hsu FC, Dana T, Fu R, Chou R. Nonopioid Pharmacologic Treatments for Chronic Pain. Published 2020. Available at: <https://effectivehealthcare.ahrq.gov/sites/default/files/pdf/nonopioid-chronic-pain.pdf>. Accessed January 19, 2021.
- ⁶⁹⁹ Kligler B, Bair MJ, Banerjee R, DeBar L, Ezeji-Okoye S, Lisi A, Murphy JL, Sandbrink F, Cherkin DC. Clinical Policy Recommendations from the VHA State-of-the-Art Conference on Non-Pharmacological Approaches to Chronic Musculoskeletal Pain. *Journal of General Internal Medicine*. 2018;33:16-23.
- ⁷⁰⁰ Kligler B, Bair MJ, Banerjee R, DeBar L, Ezeji-Okoye S, Lisi A, Murphy JL, Sandbrink F, Cherkin DC. Clinical Policy Recommendations from the VHA State-of-the-Art Conference on Non-Pharmacological Approaches to Chronic Musculoskeletal Pain. *Journal of General Internal Medicine*. 2018;33:16-23.
- ⁷⁰¹ Agency for Healthcare Research and Quality. Noninvasive Nonpharmacological Treatment for Chronic Pain: A Systematic Review. Published 2018. Available at: <https://effectivehealthcare.ahrq.gov/products/nonpharma-treatment-pain/research-2018>. Accessed January 19, 2021.
- ⁷⁰² Tang SK, Tse MM, Leung SF, Fotis T. The Effectiveness, Suitability, and Sustainability of Non-Pharmacological Methods of Managing Pain in Community-Dwelling Older Adults: A Systematic Review. *BMC Public Health*. 2019;19:1488.
- ⁷⁰³ Kligler B, Bair MJ, Banerjee R, DeBar L, Ezeji-Okoye S, Lisi A, Murphy JL, Sandbrink F, Cherkin DC. Clinical Policy Recommendations from the VHA State-of-the-Art Conference on Non-Pharmacological Approaches to Chronic Musculoskeletal Pain. *Journal of General Internal Medicine*. 2018;33:16-23.
- ⁷⁰⁴ Niknejad B, Bolier R, Henderson CR, Delgado D, Kozlov E, Löckenhoff CE, Reid MC. Association Between Psychological Interventions and Chronic Pain Outcomes in Older Adults: A Systematic Review and Meta-Analysis. *Jama Internal Medicine*. 2018;178:830-9.
- ⁷⁰⁵ Sullivan MD, Vowles KE. Patient Action: As Means and End for Chronic Pain Care. *Pain*. 2017;158:1405-7.
- ⁷⁰⁶ Wilson M, Finlay M, Orr M, Barbosa-Leiker C, Sherazi N, Roberts ML, Layton M, Roll JM. Engagement in Online Pain Self-Management Improves Pain in Adults on Medication-Assisted Behavioral Treatment for Opioid Use Disorders. *Addictive Behaviors*. 2018;86:130-7.
- ⁷⁰⁷ Centers for Medicare and Medicaid Services. CMS Roadmap: Strategy to Fight the Opioid Crisis. Published Available at: <https://www.cms.gov/About-CMS/Agency-Information/Emergency/Downloads/Opioid-epidemic-roadmap.pdf>. Accessed August 1, 2022.
- ⁷⁰⁸ United States Department of Human and Health Services. 5-Point Strategy To Combat the Opioid Crisis. Published 2018. Available at: <https://www.hhs.gov/opioids/about-the-epidemic/hhs-response/index.html>. Accessed February 15, 2020.
- ⁷⁰⁹ National Academies of Sciences, Engineering, and Medicine. Pain Management and the Opioid Epidemic: Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use. National Academies Press. 2017.
- ⁷¹⁰ National Institutes of Health. About the NIH HEAL Initiative. Published 2018. Available at: <https://www.nih.gov/research-training/medical-research-initiatives/heal-initiative>. Accessed February 15, 2020.
- ⁷¹¹ Ma J, Bao YP, Wang RJ, Su MF, Liu MX, Li JQ, Degenhardt L, Farrell M, Blow FC, Ilgen M, Shi J. Effects of Medication-Assisted Treatment on Mortality Among Opioids Users: A Systematic Review and Meta-Analysis. *Molecular Psychiatry*. 2019;24:1868-83.
- ⁷¹² Sordo L, Barrio G, Bravo MJ, Indave BI, Degenhardt L, Wiessing L, Ferri M, Pastor-Barriuso R. Mortality Risk During and After Opioid Substitution Treatment: Systematic Review and Meta-Analysis of Cohort Studies. *BMJ*. 2017;26:357.

CONFIDENTIAL

-
- ⁷¹³ Ettner SL, Huang D, Evans E, Rose Ash D, Hardy M, Jourabchi M, Hser YI. Benefit–Cost in the California Treatment Outcome Project: Does Substance Abuse Treatment “Pay for Itself”? *Health Services Research*. 2006;41:192-213.
- ⁷¹⁴ Gerstein DR, Johnson RA, Harwood HJ, Fountain D, Suter N, Malloy K. Evaluating Recovery Services: The California Drug and Alcohol Treatment Assessment (CalDATA) General Report. Sacramento, CA: California Department of Alcohol and Drug Programs. 1994.
- ⁷¹⁵ Naumann RB, Durrance CP, Ranapurwala SI, Austin AE, Proescholdbell S, Childs R, Marshall SW, Kansagra S, Shanahan ME. Impact of a Communities-Based Naloxone Distribution Program on Opioid Overdose Death Rates. *Drug and Alcohol Dependence*. 2019;204:107536.
- ⁷¹⁶ Coffin PO, Sullivan SD. Cost-Effectiveness of Distributing Naloxone to Heroin Users for Lay Overdose Reversal. *Annals of Internal Medicine*. 2013;158:1-9.
- ⁷¹⁷ Nguyen TQ, Weir BW, Des Jarlais DC, Pinkerton SD, Holtgrave DR. Syringe Exchange in the United States: A National Level Economic Evaluation of Hypothetical Increases in Investment. *AIDS and Behavior*. 2014;18:2144-55.
- ⁷¹⁸ Belani HK, Muennig PA. Cost-Effectiveness of Needle and Syringe Exchange for the Prevention of HIV in New York City. *Journal of HIV/AIDS & Social Services*. 2008;7:229-40.
- ⁷¹⁹ Delaney, J. *The Right Answer: How We Can Unify Our Divided Nation*. Henry Holt and Company, Macmillan Publishing Group. New York, New York. 2018.
- ⁷²⁰ Ballreich J, Mansour O, Hu E, Chingcuanco F, Pollack HA, Dowdy DW, Alexander GC. Modeling Mitigation Strategies to Reduce Opioid-Related Morbidity and Mortality in the US. *JAMA Network Open*. 2020;3:e2023677.
- ⁷²¹ Alexander GC, Ballreich J, Mansour O, Dowdy DW. Effect of Reductions in Opioid Prescribing on Opioid Use Disorder and Fatal Overdose in the United States: A Dynamic Markov Model. *Addiction*. 2022;117:969-976.
- ⁷²² Homer J, Wakeland W. A Dynamic Model of the Opioid Drug Epidemic with Implications for Policy. *American Journal of Drug and Alcohol Abuse*. 2021;47:5-15.
- ⁷²³ Pitt AL, Humphreys K, Brandeau ML. Modeling Health Benefits and Harms of Public Policy Responses to the U.S. Opioid Epidemic. *American Journal of Public Health*. 2018;108:1394-400.
- ⁷²⁴ Wakeland W, Nielsen A, Geissert P. Dynamic Model of Nonmedical Opioid Use Trajectories and Potential Policy Interventions. *The American Journal of Drug and Alcohol Abuse*. 2015;41:508-18.
- ⁷²⁵ Chen Q, Larochelle MR, Weaver DT, Lietz AP, Mueller PP, Mercaldo S, Wakeman SE, Freedberg KA, Raphel TJ, Knudsen AB, Pandharipande PV. Prevention of Prescription Opioid Misuse and Projected Overdose Deaths in the United States. *JAMA Network Open*. 2019;2:e187621.
- ⁷²⁶ Rao IJ, Humphreys K, Brandeau ML. Effectiveness of Policies for Addressing the US Opioid Epidemic: A Model-Based Analysis from the Stanford-Lancet Commission on the North American Opioid Crisis. *The Lancet Regional Health-Americas*. 2021;3:100031.
- ⁷²⁷ Linas BP, Savinkina A, Madushani RWMA, Wang J, Yazdi GE, Chatterjee A, Walley AY, Morgan JR, Epstein RL, Assoumou SA, Murphy SM, Schackman BR, Chrysanthopoulou SA, White LF, Barocas JA. Projected Estimates of Opioid Mortality After Community-Level Interventions. *JAMA Network Open*. 2021;4:e2037259.
- ⁷²⁸ Kertesz SG, Gordon AJ, Satel SL. Opioid Prescription Control: When the Corrective Goes Too Far. *Health Affairs Blog*. Published 2018. Available at: <https://www.healthaffairs.org/doi/10.1377/hblog20180117.832392/full/>. Accessed May 5, 2020.
- ⁷²⁹ Sullum J. New Survey Data Confirm That Opioid Deaths Do Not Correlate with Pain Pill Abuse or Addiction Rates. Published 2019. Available at: <https://reason.com/2019/08/21/new-survey-data-confirm-that-opioid-deaths-do-not-correlate-with-pain-pill-abuse-or-addiction-rates/>. Accessed May 5, 2020.
- ⁷³⁰ Volkow ND, McLellan AT. Opioid Abuse in Chronic Pain – Misconceptions and Mitigation Strategies. *New England Journal of Medicine*. 2016;374:1253-63.
- ⁷³¹ Vowles KE, McEntee ML, Julnes PS, Frohe T, Ney JP, Van Der Goes DN. Rates of Opioid Misuse, Abuse, and Addiction in Chronic Pain: A Systematic Review and Data Synthesis. *Pain*. 2015;156:569-76.

CONFIDENTIAL

-
- ⁷³² Compton WM, Jones CM, Baldwin GT. Relationship Between Nonmedical Prescription-Opioid Use and Heroin Use. *New England Journal of Medicine*. 2016;374:154-63
- ⁷³³ Jones CM, Paulozzi LJ, Mack KA. Sources of Prescription Opioid Pain Relievers by Frequency of Past-Year Nonmedical Use: United States, 2008-2011. *JAMA Internal Medicine*. 2014;174:802-3.
- ⁷³⁴ National Institute of Drug Abuse. Effective Treatments for Opioid Addiction. Published 2016. Available at: <https://www.drugabuse.gov/publications/effective-treatments-opioid-addiction/effective-treatments-opioid-addiction>. Accessed March 11, 2019.
- ⁷³⁵ Mattick RP, Breen C, Kimber J, Davoli M. Buprenorphine Maintenance Versus Placebo or Methadone Maintenance for Opioid Dependence. *Cochrane Database of Systematic Reviews*. 2014;2.
- ⁷³⁶ Alexander GC, Ballreich J, Mansour O, Dowdy DW. Effect of Reductions in Opioid Prescribing on Opioid Use Disorder and Fatal Overdose in the United States: A Dynamic Markov Model. *Addiction*. 2021.
- ⁷³⁷ United States Department of Justice, National Institute of Corrections. Cost Benefit Analysis of Adult Drug Courts. Published 2013. Available at: <https://nicic.gov/cost-benefit-analysis-adult-drug-courts>. Accessed February 15, 2020.
- ⁷³⁸ Holtgrave DR, Pinkerton SD, Jones TS, Lurie P, Vlahov D. Cost and Cost-Effectiveness of Increasing Access to Sterile Syringes and Needles as an HIV Prevention Intervention in the United States. *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology*. 1998;18:S133-8.
- ⁷³⁹ Coffin PO, Sullivan SD. Cost-Effectiveness of Distributing Naloxone to Heroin Users for Lay Overdose Reversal. *Ann Intern Med*. 2013;158:1-9.
- ⁷⁴⁰ Barnett PG. The Cost-Effectiveness of Methadone Maintenance as a Health Care Intervention. *Addiction*. 1999;94:479-88.
- ⁷⁴¹ Murphy SM, Polsky D. Economic Evaluations of Opioid Use Disorder Interventions: A Systematic Review. *Pharmacoeconomics*. 2016;34:863-87.
- ⁷⁴² Washington State Institute for Public Policy. Benefit-Cost Results. Available at: <http://www.wsipp.wa.gov/BenefitCost>. Accessed February 15, 2020.
- ⁷⁴³ Fairley M, Humphreys K, Joyce VR, Bounthavong M, Trafton J, Combs A, Oliva EM, Goldhaber-Fiebert JD, Asch SM, Brandeau ML, Owens DK. Cost-effectiveness of Treatments for Opioid Use Disorder. *JAMA Psychiatry*. 2021;78:767-77.